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THE USE OF COLLOIDAL LEAD IN THE TREATMENT OF CANCER AFTER THE METHOD OF W. BLAIR BELL¹

PRELIMINARY REPORT

By H. J. ULLMANN, M.D., Director of the Department of Cancer Research, Santa Barbara Cottage Hospital, Santa Barbara, California

OLLOWING the report of Dr. F. C. Wood (1) at the Dallas meeting of the American Medical Association, on the use of colloidal lead in the treatment of cancer, we decided that the method showed sufficient value to warrant a thorough trial. This report of our work at Santa Barbara is in no sense exhaustive but is intended to present a résumé of our observations to date in the form of a preliminary communication. As the subject is too large and has too many ramifications for presentation in the time allotted, little space will be given to discussion and none to a review of the literature. Practically everything of value on this method that has been published to date may be found in the papers of the originator, W. Blair Bell. No one should attempt the use of lead until he has studied these articles.

Bell frequently refers to the difficulty of preparing his solution and its poor keeping qualities. As soon as we attempted manufacture, we found that he was right. We made our first solutions by the Bredig method, as he did, but soon modified his technic. Bell used a current of moderate voltage and relatively high amperage. After making a few solutions by this method, we changed to a high frequency current of high voltage and

relatively low amperage. According to Svedberg (2) the high frequency arc produces smaller particles than the low frequency or the direct current. Particles of all sizes are produced but the larger are removed by centrifugalization, as must be done after sparking with any current. It was also found that it was much easier to maintain a constant arc with the high frequency than with the low.

The first preparations were made strictly after the method described by Bell (3), but they were found to oxidize and precipitate in from a few hours to a day or two. The preparation was then carried out under a layer of mineral oil, and this surface layer was carried through all the steps of preparation—sparking, centrifugalization and sterilization—up to the moment of injection. The solution was kept in ice from the moment sparking commenced to the boiling just before injection. Made and kept in this manner, it remained sufficiently stable for several days, and we were able to ship it to Dr. Soiland at Los Angeles.

As such a solution was necessarily too unstable for general clinical use, our chemists attacked the problem of increasing its keeping qualities. Dr. Fritz Bischoff, our colloidal chemist, and Dr. N. R. Blatherwick, the Director of the Chemical Laboratories of

¹Read before the Radiological Society of North America, at Milwaukee, Nov. 29-Dec. 4, 1926.

the Potter Metabolic Clinic, found that poly-hydroxy compounds would markedly inhibit the oxidation and precipitation of the colloidal lead solution. Some of these, because of toxic or other properties, were unsuitable, but fortunately glucose in the proportion of 5 grams per liter was found the most satisfactory. When glucose was added to the gelatin solution calcium was found unnecessary, in fact detrimental, and the preparation so made could be sterilized, ready for use, and kept at room temperature for from weeks to months. We stored the solution under an atmosphere of nitrogen at first but this was later found to be unneces-Solutions of colloidal metallic lead are, of themselves, sterile, but the vaccine bottles after filling were incubated at 60° C. for two hours as a precaution against contamination. It was early found that the pH of the sparking solution had a marked effect and that the optimum lay between 7.2 and 7.6. Some of these preparations kept for months and others for a few weeks only. We have not been able as yet to account for this variation.

The clinical and toxic effects varied enormously. We observed regressions, liquefactions and no demonstrable effects on the tumors in different individuals. We are not vet ready to classify the effect by the type of tumor or condition of patient and will make no attempt to do so. We have had two patients come to autopsy with marked liquefaction of metastatic foci in lungs and liver. In each of these, death resulted from pneumonitis developing about the liquefied pulmonary nodules. In one of these the large primary cervical tumors had regressed by shrinking and fibrosis until the neck was nearly normal in outline. In no case coming to autopsy where the total dose of lead was less than 200 mgm. was appreciable gross effect on the tumors demonstrated.

As Bell gives no definite information regarding the average safe initial dose a care-

ful examination of his papers was made and from the clinical reports where the dosage was given it was decided to use 1.54 mgm. per kilo of net body weight without taking the size of the tumor into consideration. After a few injections we were thankful that we had not used larger and uniform doses, for the toxic effects were, in some cases, alarming; in others, nil.

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Lumbar pain was constant, appeared a few hours after injection, and lasted from two to twenty-four hours. Abdominal pain sometimes occurred, but was far from being a regular symptom. In a few instances, a sharp chill lasting about an hour followed the injection in from two to three hours. A sharp rise in temperature—sometimes to 102° F.—was fairly constant. It appeared two to four hours after the administration of the lead and lasted a few hours. Pain in the tumor and moderate increase in size was the rule, especially after the first dose, as was nausea, vomiting, and anorexia. Hematuria was found from twenty-four to forty-eight hours after the injection in nearly every instance, but soon disappeared. An acute nephritis and fall in kidney function by the dye test was practically constant.

The blood showed the most marked and alarming of all the toxic effects. There was a primary drop in hemoglobin, followed later by the red blood cells. At times the drop was moderate, but all too frequently it was not only alarming but critical. In two instances transfusion was necessary after The hemoglobin in these the first dose. cases fell from 100 per cent to 30 per cent and from 78 per cent to 28 per cent in a week and the red cells from 4,400,000 to 2,-200,000 and from 4,700,000 to 2,200,000. Each of these patients had received 90 mgm. of colloidal lead in one dose. showed a fall of only 10 per cent, from 86 to 76, in hemoglobin, but a reduction in red cells from 5,200,000 to 2,600,000 following a total dose of 352 mgm. in four weeks. In

sharp contrast to these was a patient who had a rise in the hemoglobin from 85 to 100 per cent and at the same time a reduction of the red cells from 4,500,000 to 3,470,000. This was after a single dose of 50 mgm. Little or no effect on the tumor was demonstrated after this or subsequent doses. Stippling of the red cells was practically constant and remained a varying time. It appeared to have no relation to the degree of anemia. Sharp rises in the white count were observed in many instances but were not constant.

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From our observations of its effect to date we believe that colloidal lead should not be used if the patient is unable to stand a reduction of at least 50 per cent of his kidney function; in the presence of nephritis; if the hemoglobin is below 50 per cent or the red blood cells below two million, or if the tumor has invaded the lungs. Bell gives brain and lung involvement as contra-indications (3). We believe that while involvement of the liver is not a contra-indication, it increases the dangers of the administration.

As the toxic effects in a large majority of our cases were so alarming that we were unable to give the doses recommended by Bell, we felt that it was imperative to find a less toxic preparation. We were encouraged to go on with the work because of the marked effects on some of the tumors following moderate dosages and were disappointed at not being able to continue treatment because of the severity of the reactions or the resulting anemia.

On the hypothesis that colloidal lead is less toxic than the ionic form, Dr. Bischoff suggested that lead orthophosphate, Pb₃ (PO₄)₂, be tried. This salt is soluble only to the extent of 0.13 mgm. per liter of serum, and is the form in which lead is supposed to be stored in the bones in chronic plumbism (4). It is stable in neutral solutions but in the presence of even a slight

acidity is changed to the acid phosphate, Pb HPO₄, which is a hundred times as soluble (4).

As malignant tumors contain a certain amount of lactic acid (5) and as the insoluble salt changes to the more soluble in the presence of very small quantities of this acid, it was hoped that the tumor would be affected as by the metallic preparation without a correspondingly severe effect on the Comparative tests were made on blood. rabbits. Lead oxide colloid, 4 mgm. per kilo, produced a fall in the hemoglobin of 35 per cent in four days in one animal. An ionic solution of lead acetate, 4 mgm, per kilo: 30 per cent in three days. Colloidal metallic lead, 3 mgm. per kilo, produced an average fall of 35 per cent in four animals in from three to four days, while colloidal lead phosphate in doses from 4 to 16 mgm. per kilo had no effect on the hemoglobin of four rabbits over a period of six days. All doses are calculated in terms of lead element, not of the salt.

This preparation was then given to pa-Two of these had had previous treatment with the metallic colloid but the treatment had been discontinued because of The time has been too the toxic effects. short to draw conclusions but the apparent clinical effect on the tumors, shown by initial pain and swelling followed by reduction in size, seems to be as marked as after the administration of the metallic colloid. The toxic effects, so far, have been neg-One patient, who had not had the metallic colloid for some time and whose tumor, a cervical one, had begun to enlarge rapidly after an initial regression, has shown a steady rise in hemoglobin and red count. Previous treatment had been terminated because of the severity of the reactions and an increasing anemia. He had had a total of 289 mgm, of lead in the colloidal metallic form in four doses over a period of twelve weeks. During this time the hemoglobin was reduced from 90 to 55 per cent and the red count from 3,950,000 to 3,100,000. Two of the four injections produced a sharp chill. When he re-entered the hospital the hemoglobin was 69 per cent and the red count 3,300,000. Following five doses of the colloidal phosphate in a period of four weeks and five days, a total of 432 mgm. of lead, the hemoglobin was 84 per cent and the red count 3,650,000. The tumor is again regressing. There was no general reaction following any of the injections, but for from twenty-four to forty-eight hours after each injection the tumor enlarged slightly and became more painful.

This case is cited to illustrate the difference in the effect of the preparations described. It is too early to judge of the clinical value of either. There has been no autopsy after the use of the phosphate so that we do not know if the same marked effect on the tumors produced by the metallic colloid will be obtained. In some of the patients receiving the phosphate there has been a moderate reduction in both the hemoglobin and the red count. Stippling has been observed for a short time after injection, but was variable and usually disappeared in a few days.

There are many questions yet to be answered and we are trying to attack the problem from as many angles as possible. Interesting observations have been made on the blood chemistry but sufficient data for a report are not yet at hand. We will, how-

ever, report from time to time such observations as we believe will be of value to those using this method of treatment, and we hope that they will do the same. Data accumulated from as many sources as possible are urgently needed so that the method may be evaluated without delay and avoidable accidents with this dangerous method of treatment prevented.

We had hoped to report on the effect of radiation on tumors following the administration of lead, but our observations at the present are insufficient. ad

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THE CANCER PROBLEM WITH REFERENCE TO RECENT DEVELOPMENTS1

By M. J. SITTENFIELD, M.D., New YORK CITY

some quarters that very little has been accomplished in cancer so far. it seems to me on the contrary that valuable additional information has accumulated recently that is of paramount importance to the cancer student. Whilst we have not vet reached the very heart of the problem, at any rate the new work to be discussed here appears to have important bearing on the cancer problem as a whole. And so at this time, permit me to bring before you, what, in my opinion, are some of the outstanding new developments.

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First of all let us review the work of Warburg and his collaborators regarding the metabolism of the cancer cell. point of departure for these studies was an earlier observation that respiration in the sea urchin egg during fertilization was six times as great as that of the non-fertile egg. Extending these studies still further he devised most accurate methods for measuring respiration and oxidation of normal tissues, at work and at rest, with a parallel series of studies on rapidly growing tissue, such as embryonic and tumor tissue. To his great surprise, he found that respiration of the Flexner-Jobling carcinoma in Ringer's solution was decidedly less than that of the liver, spleen or kidney of the rat. Here, in other words, conditions presented themselves which indicated that tumor tissue either lacked or was deficient in something that was necessary for combustion. In the search for an explanation of these unsuspected findings, he added glucose to the Ringer's solution, and found that respiration was depressed still further and was practically brought to a standstill. Attempting to as-

ESPITE the opinion that prevails in certain the true significance of this, he discovered that the metabolism in the cancer tissue differed from that in normal tissue. inasmuch as in the normal cell, respiration takes place by oxidation, whilst in the cancer cell, metabolism is carried on chiefly by the splitting of glucose into lactic acid. make certain of his ground, he checked up his controls-kidney, liver, and spleen-and in these only very minute or negligible quantities of lactic acid were found. Further investigation revealed that cancerous tissue liberates 12 per cent of its weight as lactic acid within an hour, also that in a given measured time, tumor tissue produces a hundred times as much lactic acid as blood. two hundred times as much as frog muscle at rest, and eight times as much as the same muscle working to the limit of its capacity.

The glycolytic activity in tumors can be demonstrated for days, if the tumor be kept in sterile Ringer's solution at body tempera-If fragments of tumor kept under these conditions for three days are transplanted into a normal rat, a tumor will still develop. On the other hand, when the glycolytic activity of the tumor is inhibited, by freezing in liquid air, for instance, though the tumor tissue is still alive, it will no longer be able to produce a tumor upon transplantation. In the case of rat carcinoma, for instance, the ratio is 4 molecules of lactic acid for every molecule of oxygen consumed, and the same, of course, holds true for human carcinoma. The fact that malignant tumors produce three to four times as much lactic acid per molecule of oxygen consumed as benign tumors seems of the greatest significance, and, according to Warburg, the difference between malignant and benign tumors is one of degree rather than of kind.

¹Read before the Radiological Society of North America, November 30, 1926, at Milwaukee, Wis.

It is not the scope of this paper to discuss at length all the significant work that has appeared recently, but only to touch some of the high spots. In a personal interview with Gve last summer, he impressed me as just as enthusiastic and firm in his stand as when his first paper came out. His latest experiments seem to confirm and substantiate his original investigation. experiments, reported a year ago, suggest though by no means demonstrate that we are dealing with an infectious agent of some sort, which evidently does not fit our orthodox notions of infectivity. Results of later experiments along similar lines corroborate Gve's results even if they do not admit the existence of two special factors. But whatever may ultimately prove the real agents in the filtrate, the credit is due to Gve's ingenious and tireless persistence in the search for one or more factors necessary to produce neoplasia. From personal experience, now confirmed by others, it is obvious that the slightest error in this most complicated technic will make a would-be positive outcome negative. Hence, various negative results that have been reported lately may rest upon slip-ups in the experimental conditions. I have reason to state that additional evidence of Gve's contentions will appear shortly to satisfy even the most critical cancer student. Whether these causative agents will eventually explain the entire question of cancer etiology is difficult to foretell. The main conclusions, however, drawn from his and my own experiments, indicate the infectivity of a cell-free filtrate in the production of the Rous chicken sarcoma and also in that of the Mouse Sarcoma 37.

Another important contribution is the work of Burrows,² the result of many years' intensive research. Unfortunately this opportunity does not permit me to describe the mechanism and details of his work.

Suffice it to say briefly that he and his co-workers believe that cancer is the result of a local vitamin imbalance in the organism. He infers that oxygen deficiency and disturbed metabolism of the tissues through the lack of proper blood supply, lower the Vitamin A content of the tissue, and thus allow an accumulation of Vitamin B. The same author implies that Vitamin A conforms to the growth-inhibiting, and Vitamin B to the growth-activating substance in the organism, and we are looking forward to further experimental evidence to establish the relationship of these substances to cancer.

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Perhaps the most talked of new development in cancer is the recent communication of Blair Bell regarding the intravenous injection of colloidal lead in cases of advanced cancer. This has aroused so much interest in the cancer world that I felt personally the need to get first-hand information at his clinic in Liverpool last summer. Out of 227 patients treated by him within the past five years, he claims there are 50 in whom the disease has been clinically arrested for anywhere from one to five years. In view of these claims it seems desirable to repeat some of his experiments, but, up to the present, my own experience clinically and experimentally is not of sufficient range to permit me to state definite conclusions of my own. Blair Bell stresses the close identity between the chorionic epithelium and the malignant cell. According to Bell the chorionic epithelium is a normally malignant cell until it comes under systemic control. It is malignant, he argues, before it links up with the maternal tissue insofar as it is dependent upon its own efforts to obtain nourishment for itself. In the course of another investigation he demonstrated some time ago that one-half the lethal dose of lead in colloidal form induced abortion in pregnant rabbits, by coagulation necrosis which was limited strictly to the cells of

²The Effect of X-rays on the Vitamin Needs of the Organism and Cancer. M. T. Burrows, L. H. Jorstad, and Edwin C. Ernst, Radiology, October, 1926, p. 279.

the chorion. Without here taking occasion to enter into the consideration of the merits or demerits of his views regarding the actual correlation of the chorion epithelium with the malignant cell, evidence is adduced by him in the fact that both types of tissue show an increase in the phosphatide and in the phosphatide-cholesterol ratio. similarity of both types of tissue in their increased glycolytic activity and physicochemical reactions, and also in the sensitiveness of both to colloidal lead, suggests to him a close biological relationship. According to Blair Bell, in each of these tissues lead appears to produce coagulation necrosis, providing it is able to reach the cells in sufficient quantities. The action of lead, therefore, is quantitative: in other words, it is necessary that sufficiently large doses of lead be administered to affect the malignant tissue without causing lead toxemia. It is of particular interest in this connection to note the great difference in individual susceptibility to the effect of lead. From clinical observation of such it would seem that there is some sort of relationship between the size of the tumor and the quantity of Some individuals tolerate lead absorbed. very large doses without difficulty, others again are poisoned by very small doses. It is assumed that the action of lead is exerted chiefly upon the capillaries of the growth; hence, upon the malignant cells locally, without seriously involving the other tissue.

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The first phenomenon to be recognized after the injection of lead is an intense congestion followed by edema and definitely recognizable hyperplasia of the tumor. Thrombi are found in the tumor capillaries, shutting off the blood supply of the tumor. As a result of this vascular starvation, necrosis takes place, then absorption, and finally shrinkage of the tumor.

From this brief histological description, it would appear, according to the Liverpool school, that the lead is stored up in the

tumor far in excess of that found in normal tissues or organs. So far, then, this may very well be the case, but keep in mind that lead, to be effective, must be given practically in lethal doses. Lead toxemia is the greatest stumbling block in this work, as the kidney, blood, and blood-forming organs, also the cerebral and gastro-intestinal systems suffer profound injury. Kidney impairment, with depressed excretion or even suppression, very frequently follows repeated small doses-more so even than the single large dose of lead. Casts and albumin in the urine must be carefully watched for during the treatment, and chronic nephritis. therefore, is one of the first contra-indications. The blood and blood-forming organs sustain severe damage, and in cases where the hemoglobin is 50 per cent or below, or the red blood cells three million or below. the lead injections must be discontinued. In fact, during the treatment the daily picture of the blood must be rigidly studied, and stippling of the red cells, more than one to a field, is a danger sign, designating that treatment cannot be resumed until the stippling disappears. Cerebral or lung metastases are other objections to the treatment, and retinal involvement frequently goes hand in hand with renal disturbances. Aside from the acute lead poisoning there is also a hazard of chronic toxemia, as you will recall that the effect of lead is cumulative. and hence latent symptoms may occur at any time after several months. In Liverpool they told me they had observed it even a year after the treatment, in the form of blindness and paralysis of the lower extremities.

With this clearly in mind it is easy to understand that the lead treatment as we know it now applies only in cases of advanced and non-surgical cancer, and then only in conjunction with X-ray and radium. The great difference in the susceptibility to lead poisoning makes it particularly hazard-

ous for the beginner, and necessitates expert clinical experience. Morover, unless you are able to obtain a standard stable preparation of colloidal lead from a reliable source, it is necessary to prepare it fresh and use it within six to twelve hours.

The method of preparation that I saw in Liverpool and which I follow here, is that of electrolysis of assay lead. The pure assay granular lead in 0.5 per cent gelatin is sparked across by means of lead electrodes for ten to fifteen minutes with about 70 volts and 20 amperes. The metallic lead is thus converted into a suspension of colloidal particles, and then centrifuged for three minutes at 1,700 revolutions per minute to throw down the coarser particles which have not gone into suspension. The supernatant fluid is then placed in a beaker and heated for a few minutes to 100° C, to drive off the oxygen and sterilize the solution. For commercial purposes it is put up in 25 c.c. ampoules in an atmosphere of nitrogen, and under these conditions it will keep two to three months. In Great Britain, the British Colloid Company is distributing it to clinical pathologists who have taken Blair Bell's course and have gained the necessary experience.

In this connection it is desirable to draw attention to the fact that the stability of the colloidal solution has perhaps a great deal

to do with the absorption of lead in the system. Martland, in a recent communication. reported that a highly stable colloidal lead preparation used by him failed to induce the slightest effect on the tumor in 15 cases treated: in fact. 13 of these died from severe lead poisoning. From his histological findings, none of the lead seemed to have reached the tumor. It was taken up by cells of the reticulo-endothelial system, as the phagocytic cells in the spleen, liver and bone marrow were loaded with lead particles. In explanation of these findings it would seem that the lead in his preparation was perhaps so stable that it failed to dissociate itself. and hence acted as a foreign body. It seems to me that it will be essential, in the first place, to have the best sort of co-operation in the preparation of a not too stable solution of lead, one that will be taken up and absorbed by the tumor, and secondly, that the agent be non- or very slightly toxic to the rest of the body.

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Perhaps it would not be amiss right here to suggest that it would be unwise for the present to publish clinical results unless an appreciable time has elapsed. The intravenous injection of colloidal lead as it is used now is accompanied by considerable danger, the result of which may be very distressing to the patient, and so, to the cancer specialist.

THE METALLIC COLLOIDS IN THE TREATMENT OF CANCER¹

(A PRELIMINARY REPORT)

By ALBERT SOILAND, M.D., WILLIAM E. COSTOLOW, M.D., and ORVILLE N. MELAND, M.D., Los Angeles, California

DURING the past year we have been supplementing our regular treatment of malignancy by radiation with the use of colloidal metals. The number of patients we have observed has been sufficient to warrant an attempt to evaluate this method of treatment by careful clinical observation. The metals used have been gold, copper, and lead. Of these, the patients receiving lead have been most carefully observed since Blair Bell reported such good results in the use of that metal.

COLLOIDAL GOLD

Quite a number of patients have had colloidal gold, the preparation being that advocated by Ochsner. In these cases the gold was taken by mouth and mainly used prior to their radiation treatment. In no case was there any apparent effect on the growth. One of the patients who had an advanced carcinoma of the breast said that her appetite became better, and her pain lessened to such an extent that she could sleep. Another, who had an extensive carcinoma of the cervix, and who had had a thorough course of radium elsewhere, had been given colloidal gold, but it had produced so much gastric distress that it was discontinued.

COLLOIDAL COPPER

Colloidal copper was used intramuscularly in four recurrent post-operative breast cases and in one case of late metastases in the inguinal glands following removal of a carcinoma of the bladder. All of these cases were heavily treated by X-radiation and radium. In none of the cases was there any apparent effect on the growth except in the

one patient with the inguinal involvement, which diminished to about one-third its original size, followed by a severe, continuous pain in the region of the tumor, terminating in a generalized rapid metastasis, with death in six weeks. Other cases had sporadic copper treatment without apparent benefit, and becoming discouraged with this metal, we discontinued its use.

COLLOIDAL LEAD

Blair Bell's contributions on colloidal lead have been eagerly followed by many, and one of us (O. N. M.) has made a special study of all the factors which Bell has brought out in his various communications, so that we have approached the therapeutic use of this agent with a fair knowledge of the requirements and attending responsibilities. Our cases to date are not many and this report is to be considered strictly a preliminary one, covering only our own individual limited experience with colloidal lead. Our results so far are disappointing, vet when we consider the newness of the method and that the time is too short either to approve or condemn, we are not without hope of better accomplishments as we become more familiar with the subject in toto.

We have so far treated twelve patients with lead, furnished us through the courtesy of Dr. Ullmann and Dr. Bischoff, of the Santa Barbara Cottage Hospital. These were all post-operative recurrences, or cases radiated to the saturation point, and hopeless from any other therapeutic viewpoint.

A brief résumé of the case records is presented.

Case I. Mrs. M., age 50, weight 150 pounds. Recurrent carcinoma of left breast,

¹Read by Dr. Soiland before the Radiological Society of North America, at Milwaukee, Nov. 29 Dec. 4, 1926.

with metastases to subra-clavicular glands of the same side and extension into the right breast and axilla. She received two thorough courses of radiation, with improvement for three months, after which there was a rapid return of activity. She was given two massive doses of lead, totalling 180 mgm.—ten days apart. Both injections were followed by severe nausea and vomiting and a prostrating backache. The second dose produced a progressive secondary anemia, making it necessary to resort to transfusion. There was also a marked destructive effect on the kidneys, so much so that the urine was constantly loaded with albumin, casts, and red cells. The anemia gradually disappeared, but the kidney condition became more and more progressive so that no further treatment could be given. The growth diminished rapidly in size, some nodules became discrete, soft, and almost disappeared. After discontinuation of the treatment, however, growth recommenced and the patient is getting progressively worse.

Mrs. C., age 34, weight 97 Case II. Recurrent carcinoma of right breast following operation three months previously. There were subcutaneous nodules over the anterior portion of the chest and in the axilla. She had received two courses of X-radiation over the site of the recurrence, with some temporary improvement. She was then given two injections of lead totalling 73.5 mgm. There was no general reaction, but a marked drop in red cells took place. One week later a lead encephalopathy developed, with a suicidal tendency. The nodules took on renewed growth and death ensued from liver involvement.

Case III. Mrs. H., age 38, weight 120 pounds. Recurrent adenocarcinoma of left breast following radical operation four months previously. She had been given two thorough courses of X-radiation, but there was a recurrence in the chest wall along

the costochondral junction of the fourth and fifth ribs. There was also a distant metastasis to the fifth rib posteriorly. A total of 120 mgm. of lead was administered in three doses at three-week intervals. A moderate anemia resulted which was of no importance. There was a temporary improvement in the recurrence, but three months after commencing the lead she had pleural metastases, with an effusion into the left chest. A generalized edema and a myocarditis came on, which resulted in a cardiac death.

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Case IV. Mrs. S., age 62, weight 180 pounds. Post-operative adenocarcinoma of the left breast from which the surgeon removed only a small local growth. Following histologic examination, he inserted four radium needles and a few X-ray treatments were given. On being referred to us, we administered a thorough course of X-radiation to the entire left breast, but the growth. which was localized in the scar, grew continuously. She was given 142 mgm. of lead in two sittings, with no general reaction, but with some disturbance of kidney function. However, growth was continuous and the patient discontinued treatment. The last examination showed that the newgrowth had increased to four times its original size.

Case V. Mr. O., age 46, weight 220 pounds. Osteosarcoma of right femur involving the entire bone, which has increased to four times its regular size. He was given two treatments, totalling 247 mgm. of lead. There was no reaction save profuse perspiration and a moderate anemia, which gradually cleared up. Two courses of X-radiation were given, with an apparent arrest of growth in the upper portion. Patient is still under treatment.

Case VI. Miss O'C., age 49, weight 150 pounds. Carcinoma of right breast with massive metastases into the supraclavicular and axillary nodes. She was given two courses of X-radiation with only slight im-

provement. Because of a high blood pressure which presaged a kidney impairment despite a normal urine and functional test. and also because of the possibility of a right-sided pleural involvement, only 45 mgm, of lead was given at the first sitting. There was no general reaction, but a drop of 12 per cent in hemoglobin took place. Twelve days later, when apparently everything had cleared up, she was given 87 mgm. of lead. She had a severe chill, perspired freely, vomited, and her temperature shot Respiration became rapid and she became severely jaundiced. A persistent backache came on and only 60 c.c. of bloody urine was excreted. The urine cleared up in color but decreased, and there was finally complete suppression. The right chest filled up with fluid, so that 1,500 c.c. was removed. The involved breast became very tender and decreased greatly in size, while the lymph nodes in the supraclavicular and axillary regions became smaller and more discrete, whereas before they were hard and confluent. Death took place on the sixth day from the pleural involvement and the anemia.

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Case VII. Mr. G., age 66, weight 170 Carcinoma involving the pelvic organs, with metastatic glands in the right inguinal region. Biopsy at the Mayo Clinic established the diagnosis, where radium and X-radiation were applied with a great deal of benefit. A year later there was a recurrence of pain, but no relief was obtained following a second series of X-radiation. He was given an initial dose of 68 mgm. of lead which was followed by a severe local pain, secondary anemia, and nephritis. The recovery from the administration of the lead was very slow, and as we were unable to assure the patient of any permanent results, he discontinued the treatment.

Case VIII. Mrs. H., age 68, weight 150 pounds. Carcinoma of the cervix with massive extension into the pelvis involving the

posterior vaginal wall and rectum. Four months previously she had had a course of radium elsewhere, with no benefit. complained of continuous pain in the rectum due to a large mass almost occluding its lumen. She was given two injections of The first one, of 52 mgm., resulted lead. in no general reaction, but there was a marked diminution of pain in the rectum and a shrinking of the mass to about onehalf of its original size so that for the first time in three months she was having normal stools. The second, of 87 mgm., produced a severe local pain, an agonizing backache, a moderate anemia, and a marked The symptoms gradually disappeared except that there was always a feeling of soreness in the rectum. About two weeks after her last treatment she developed a rectovaginal fistula. The induration in the pelvis decreased in amount, and the pain was much less when the stools were of the proper consistency. Her general condition was good, but no further treatment was advised on account of increasing the size of the fistula. Whether the fistula came on as a result of her former radium therapy or as a result of the lead breaking down the malignant tissue in the rectovaginal wall, we are at a loss to say.

Case IX. Mrs. W., age 56, weight 120 pounds. Carcinoma of the cervix, with extension to the bladder and rectum. year previously the patient had had a pelvic operation which consisted of a suspension and oöphorectomy. Ten months later radium had been applied for an irregular uterine bleeding, at which time 100 mgm. were applied with some improvement. When referred to us she had a frozen pelvis. Her condition was poor because of the continual hemorrhage and the recent loss of weight. She was given 70 mgm. of lead. She developed a severe chill, profuse perspiration, agonizing backache, and suppression of urine, despite an apparently normal

kidney functional test. Cyanosis, with a failing heart, came on, which responded to stimulation for a short time, but she became weaker and died 48 hours later from cardiac failure.

Case X. Mrs. M., age 68, weight 141 pounds. Post-operative adenocarcinoma of the right breast, with supraclavicular metas-She had been given a number of series of X-radiation following her operation four years previously. At first she was relieved but of late there had been a constant pain in the arm, associated with an enlarging supraclavicular mass of the right side. Thirty milligrams of lead was given as an initial dose, because, even though there was a normal kidney excretion and blood, there was a urea estimation of 40 mgm. per 100 c.c. There was no reaction except a mild secondary anemia. Ten days later 40 mgm. was given again, with only a slight backache resulting. Up to date there has been no change in the condition of the growth. She continues to use morphine as before. Still under treatment.

Case XI. Mr. M., age 80, weight 170 pounds. Carcinoma of left tonsii, with ulceration extending onto the soft pulate and down onto the tonque. Metastasis to the glands on the left side of the neck, the growth being 8 cm. in diameter. The condition is complicated by lues, for which the patient has received neosalvarsan for six months, with no improvement. He has had several high voltage treatments, with no change, except that the glands over the neck are breaking down. Received three doses of lead, totalling 100 mgm., with no reaction. Larger doses were not given because of fear of edema of the throat and glottis. Patient still under treatment.

Case XII. Mrs. F., age 60, weight 155 pounds. Carcinoma of cervix, with extension onto the anterior vaginal wall and into both broad ligaments. Given, 1,200 mgh. of radium in vagina, with considerable re-

action; more not given because of fear of producing a vesicovaginal fistula. Two injections of lead, totalling 76 mgm., given, with little reaction. No change in growth.

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In reviewing the cases cited, we are rather disappointed in our results. In the colloidal gold series there has been no apparent change in the disease, though one patient maintained that there was an increased appetite, and a diminution of pain which resulted in undisturbed sleep. Concerning copper, a marked diminution in the size of the tumor took place in one individual, but with it came an increasing amount of pain and rapid metastasis. What relationship the injection of copper had to these phenomena is difficult to say, except possibly it may have had a destructive effect on the defensive forces of the body. Of those patients having colloidal lead, only two-Case V and Case VIII—showed any apparent improvement. All the others became progressively worse and in two cases death was undoubtedly hastened as a result of the treatment. Whether this was due to the extreme toxicity of the drug or to the unsuitability of the patients is questionable. However, in justice to the treatment we wish to say that all of the cases were apparently hopeless insofar as any other treatment was concerned. Many of them had been operated on by competent surgeons, and all had been exposed to heavy radiation. (A possible explanation of the failures may be due to radiation which had destroyed enough capillaries to prevent the lead from coming in direct contact with the remaining malignant cells.)

The method is dangerous, since the lead is exceedingly toxic. If used in the large doses, as Bell recommends, the reaction is very severe, while if used in smaller doses it results in a chronic type of lead poisoning, as shown by a progressive secondary anemia, and a chronic nephritis, with the urine diminished in quantity and loaded with albumin and casts. If the large doses are given, the patient goes through a regular reactive sequence.

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There are no particular symptoms for at least thirty minutes after the injection of the lead, when the patient begins to complain of a tingling sensation over the body. This is followed by a profuse perspiration and a nausea, which increases to the point of vomiting. This may keep up for two or three days, but in no instance has there been any evidence of abdominal pain or colic. Usually in an hour there is a severe backache, evidently due to a congestion of the kidneys. The urine diminishes in amount, and, when passed, is red in color from the red cells present, and contains an abundance of albumin and casts. In two cases, the effect on the kidneys was so severe as to result in complete suppression. As was mentioned above, the blood cells are attacked. The white cells diminish but regenerate in a short time so that the leukopenia is followed by a mild leukocytosis. The red cells are quickly destroyed, producing an anemia, which may be so severe as to necessitate transfusion for recovery. This happened in one of our cases. The day following the injection, the scleræ are mildly jaundiced, due to red-cell destruction as well as liver destruction. Unfortunately we were unable to obtain autopsies in the cases of the patients who died, so we cannot give the distribution of the lead in the organs of the body.

A few patients complained of localized pain in the tumor area; most of the time it was mild in character, though in one (Case VIII) it was so severe that it required the use of morphine. In this one case, there was a rapid diminution in the size of the tumor.

From the account given of the reactions, it is obvious that it is necessary that the pa-

tients be in good physical condition and that the blood and kidneys be thoroughly investigated. The patients must be hospitalized and a complete blood examination as well as a complete urinary examination is essential. This includes not only the analysis of a 24-hour specimen of urine, but a functional test, and, in case of doubt, a blood urea test. Even these precautions may not forestall disaster, since there is no way of telling how any patient will react.

When to repeat the treatment must depend on the condition of the patient. Usually it is best to wait until all evidence of lead intoxication has disappeared. urine should be normal in quantity and free from red cells and albumin. The functional test should show at least 45 per cent. The blood should not show more than 10 to 15 per cent reduction in hemoglobin. An index of excretion and mobility of the lead is We feel that if more than one cell is seen in three or four fields, it is best The patient's appetite should be to wait. normal again and there should not be any residual weakness as a result of the former treatment. Just how long this takes is purely an individual problem; some patients are entirely well in a week, whereas others have not recovered in five weeks' time. This was especially shown in Case VII.

The dose is also important. We have tried both the massive dose, recommended by Bell, and the divided dose. The former resulted in two disasters, while the others have had very little apparent effect. If the effect of the treatment is quantitative, it is reasonable to assume that, other things being equal, there should be little difference. In order to obviate any bad effects and to immobilize the lead as soon as possible, the patients are instructed to drink an abundance of water, to take at least a liter of milk daily, while, for some, calcium is prescribed.

We are still continuing the treatment, endeavoring to determine which type of carcinoma will respond and which one will not. One of the disappointments is not only the destructive action on the blood and kidneys, but the apparent contra-indication of the drug in those cases where there are metastases to the lungs and liver. These are the cases where one would wish the treatment could be applied, since it is only through the vascular system that these cells can be reached with any assurance of success.

The dozen cases just recorded were subjected to intravenous injections of basic colloidal lead, which is, as already stated, highly toxic. A careful survey of these cases forces us to the conclusion that lead in this form cannot be exhibited to the patient in doses recommended by Bell without grave danger. This lead has been prepared by a highly skilled colloidal chemist, exactly after the formula laid down by Bell, so we are at a loss to account for the highly toxic reactions. Even in amounts approximately one-half of those used by Bell, the effects were extremely grave. The thought has occurred to us that perhaps we may have overlooked one of the details in the preparation of the lead or that Bell has not succeeded in making clear to us one or more of the intricate factors which go to make the preparation and its use complete. our chemist has succeeded in stabilizing a colloidal lead which appears on short acquaintance to possess most of the desirable qualities of the basic lead without so much detrimental action on the blood and kidneys. We are now carefully administering this type of lead to all our recent cases.

When we seriously consider the limitation of surgery and radiation in systemic cancer, we are surely justified in accepting any proffer of help, insecure as it yet may appear. We must, however, accept statements of fact when announced by such men as Blair Bell and his associates whose investigations and labors with colloidal lead over a period of more than six years would

seem to have placed this agent beyond the experimental stage. Hence, we are going to carry on our studies with colloidal lead, and we believe from our own experience with radiation and its effect on tissues, that we can time these relative agents in such a manner as to secure from each alone or in combination better results than we have been able to secure in the past. We will deem it a privilege to bring the results of this work to your attention as soon as sufficient data have been accumulated.

DISCUSSION

DR. R. H. STEVENS (Detroit): I was very sorry that Dr. Sittenfield did not have a little more time at his disposal, in order that he might go into the subject of cancer a little more thoroughly than he did. I may not, perhaps, have gotten just the idea that he wished to convey, but I had the impression that he was emphasizing the germ theory of cancer, about which we have so much controversy and discussion at the present time. It seems to me that we must keep rather open minds on this question at the present time, because there is so much evidence against this theory. I think we know at least some of the causes of cancer; we do not have to go into bacteriology in order to find them. Cancer has been produced experimentally by rubbing tar under the ears of rabbits and we see similar cancers in the industries-in men who are working in tar, men who are working in paraffin, men who are working as chimney sweeps in the old country. They develop irritation cancers in parts of the body where these irritations take place-cancers which apparently have no relationship whatever to bacterial infection. Bacterial infection is a form of irritation, and so we get back to the old irritation idea of cancer, and it may be bacterial or chemical or traumatic. So I think we must keep open minds upon this

subject. I enjoyed Dr. Sittenfield's paper very much, and especially the part relating to his experiences with the Blair Bell lead treatment, which, it seems to me, is very difficult and dangerous of application at this period of our knowledge of the subject. I talked with Dr. Leitch recently, of the London Cancer Hospital, and he denounced the treatment very strongly, while Francis Carter Wood seemed to think there might be a good deal in it. I have had no experience with it and so I can say nothing for or against it.

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Dr. Douglas Ouick (New York): This subject of the use of colloidal lead brings up a discussion of a new method, or perhaps it would be better to say the discussion of a new phase of an old method, and of course we must approach it with open minds. I think that Dr. Soiland and Dr. Ullmann are very much to be congratulated upon the note of optimism which they seem to bring with them in attempting this work. I do not know whether it has to do with the longer summer season on the West Coast than we enjoy in the East, or not, but apparently their experience is a little more optimistic than that wee bit which we have had. say we must approach it with open minds, because, after the wide publicity which was given Blair Bell's publication, no matter what our notions may be, it is one of those things that must be investigated very carefully before we express an opinion one way or the other. Right at the offset there are various factors against it. In the first place, the uses of colloids in their many forms have been gone into years ago, and I think quite thoroughly. The work with which I am most familiar at first hand is that of the late Dr. Richard Weil, in which he decided that colloidal copper was the most valuable. But summing it up in the end, he felt that the benefit derived from the colloid was not enough to compensate for the damage

done by its use. A superficial survey, at least, of colloidal lead at the present day, indicates very definitely that it is certainly a better preparation than the colloidal copper of twelve or fourteen years ago: still, it has one thing, on the face of it, against it; that is, it has no specificity at all—it is purely, as nearly as we know, a straight toxic agent. It is a question of whether or not the body can stand enough of it to kill the tumor without killing the patient, and that, of course, places it in an entirely different light from certain of the specific, yet toxic, therapeutic agents which we employ in everyday medicine.

The type of preparation I do not think I am at all competent to discuss. My feeling is that if we are going to attempt duplicating this work, we ought to stick as closely as we can to the general principle of preparation which Blair Bell used; that is, if any one knows exactly and in detail what that was. A good many of us think we know almost, pretty nearly, etc., but whether it is the real thing or not, that is a question. Of course, varying it for the sake of improvement is to be commended, and I think Dr. Ullmann is fairly on the right trail in the change which he has made. I am not taking a wallop, Dr. Ullmann, at your improvement in the preparation; I am referring to the many and varied thoughtless changes in the preparation that have apparently been made by a good many people in trying it out. Unfortunately in many instances they are made in a rather haphazard fashion.

Like every one else, I suppose, we have made a few changes in that preparation which we are using. We found, for instance, that the gelatin apparently had something to do with the sharp, immediate reaction within a half-hour or an hour after injecting it, and we have a preparation now which is free from gelatin. Then the nature of its action came up. All we can say

is that it is a straight toxic reaction, pure straight lead poisoning, and if we can hit off just the right spot, in a certain number of cases, perhaps the patient will survive and the tumor will disappear. That is not the hope we had in mind when we started quietly using it at the Memorial; we had hoped that it might bring about certain changes which would render radiation more effective. We have not been rewarded with any cheerful results in that direction as yet. and it brings up the question of just what does happen. Is not what we have heard of the beneficial effects of combining the two, open to a certain amount of conjecture. at least? Is it purely the summation of the effects of the two toxic agents? Or may we hope to have the biological effect of radiation enhanced by the effect of lead? If it is the latter, then it is very well worth considering and carrying on with; if it is the former, we may as well have a full dose of one as two half doses of the two.

Perhaps it is best for me not to say anything of our experience. You may have thought that our experiences were not at all cheerful, and they were not. I must admit that I have not seen a single case of the small group we have treated wherein I could feel that any real benefit at all could be laid at the door of the lead. We have gone through a good many of those unhappy, unfortunate experiences that center around the use of any new agent. We have seen a patient receiving 75 milligrams of lead die within twenty-four hours from kidney lesion, and at autopsy we have seen the kidney filled with hemorrhagic infarcts and all that, showing acute damage to the kidney. We have seen lesser but just as effective kidney damage. After all that, I think if we are to use the preparation and try to find out where it belongs, we must not use it on the eleventh-hour cases; we must perhaps select patients who we feel more or less certain can carry on for six

months under their own steam. There is no use trying it on someone who is going to die day after to-morrow. We must be certain of the patient's kidneys and vital functions, and try it on those who, under any circumstances, would live for a period of months; in other words, we have to select our cases more carefully.

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DR. WALTER C. ALVAREZ (Rochester. Minn.): It seems to me that one of the main problems is to estimate the resistance of the individual to the lead before it is As Simon Flexner has pointed out recently in a most stimulating article in the American Journal of Medical Sciences, different strains of mice or guinea pigs not only possess widely different resistances to infection with paratyphoid bacilli, but these resistances are non-specific; that is, it can be shown that the resistance or susceptibility to bacterial infection in the various strains or individuals runs parallel to a resistance or susceptibility to poisoning with mercuric chlorid.

It seems to me, therefore, that we might gain some idea of the way in which a patient is going to react to the lead by first determining his susceptibility to a number of less toxic drugs with definite and preferably measurable physiologic actions. extensive experience with lead poisoning has convinced me also that the marked variations in susceptibility seen, for instance, in painters, depends largely on the efficiency of the kidneys. There stands out in my memory the case of the nephritic bartender, who, in 1919, put away his apron and went to work making storage batteries. Six weeks later I was explaining to the industrial insurance commissioners why he had died of acute lead poisoning while his fellow-workmen went on, with a little anemia and an occasional attack of colic. It would be well, therefore, before treating cancer patients, to estimate the amount of effective renal tissue that they have left; and, so far as I know, that can best be done by determining the Addis-Van Slyke urea excretion quotient. The dye excretion test alone is not trustworthy.

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DR. A. BOLLIGER (Detroit): The colloidal lead treatment has been used in twelve cases in the surgical service of the Henry Ford Hospital, and the experience was not quite so bad as that which has been reported so far this evening. Among these twelve patients none died acutely. Further, none of the deaths were due to lead poisoning. Doses as high as 150 milligrams in one injection were given and patients who received 150 milligrams are still living, about two months after the injection. A solution of colloidal lead which was stabilized by adding glucose was also used experimental-This solution was much more ly in dogs. toxic than the colloidal lead solution as described by Blair Bell. Only black solutions were administered, the light colored solutions containing more or less lead carbonate or lead oxide were discarded. Then, only fresh solutions were injected. A solution is made up and injected within the hour. So far, there are no cures. One case of rapidly growing squamous-cell carcinoma seems to be definitely arrested.

Dr. W. H. Wallace (Brooklyn, N. Y.): I might as well start out by saying that I do not know a thing in the world about colloidal lead and these injections. It was interesting to me from the point of view of what might happen if we were able to inject into the tissues of a body some metallic substance that afterwards we might use for producing secondary X-rays in the tissues. Those of you whose experience goes back to the days when we were "deviled and damned" with the polarity of the static machines, will remember that we had a much better effect on skin tissues with a soft tube

that was charged by the high potential of a static machine with very low amperagemuch lower than we get to-day. There are a number of men in this Society who have called my attention to that, and it is observed generally that the higher the power of our machines (amperage) the less has been the effect on skin tissues. I think that is due to the fact that the beta rays, after all is said and done, were and are the chief rays instrumental in destroying the growths. In other words, they had an inhibitory effect on cancer tissue, if you could get them into the cancer tissue. True, you could not get them very deep; consequently the effect was mostly on the superficial epitheliomas. Now, if you can go to work and use colloidal lead or colloidal gold and from your primary rays of X-ray or radium, so that your gamma rays hit the metal and start secondary rays, I do not think there can be any question but that you are developing a great many beta rays in the tissues. and, as a consequence, this thing may be put over. Men have told me that they have radiated their cases first and given the colloids afterwards, and it seems to me that that is putting the cart before the horse, because you are all aware that one of the primary actions of the X-ray on the tissues is to close up your lymphatics, and, if you do that, your colloids are not going into the growth, because they are already, to a certain extent, closed up by whatever the proliferation may have been that caused the growth. That is the only point I have to bring out, that if you can use it in a moderate dose that will not poison your patient and then use your ray, I think possibly you may have something valuable. If somebody has done that already, I will be glad to hear his report.

Dr. SITTENFIELD (closing): I fear that Dr. Stevens did not get the main points of my paper. Owing to the short time at my

disposal, I could do little more than outline the outstanding points, and so I may not have made myself sufficiently clear. What I really meant to convey was the infectivity of the filtered tumor fluid in the production of the Rous chicken tumor, and also of Mouse Sarcoma 37. By "infectious agent" I.do not mean bacteria in the ordinary sense of the word, but an agent present in the filtered fluid, which, when injected into another fowl of the same species, will reproduce exactly the same type of tumor. Rous, in 1911, had already demonstrated that he was able to transmit a sarcoma in a chicken by means of a filtrate, and at that time he called the causative factor an "infectious agent." Gve extended these studies still further and was able to demonstrate two separate agents. The one, in his opinion, conforms to an ultra-microscopic virus, which he is able to destroy by chloroform or antiseptics. The second factor or chemical agent he calls the "specific factor," and demonstrates still further that exposure to air destroys the unstable chemical agent. The two factors, in his opinion, must be present for tumor formation and his experimental evidence bears out his contention. To illustrate: if he destroys the virus in one filtrate by chloroform, he renders the fluid innocuous; that is, no tumor will result after the injection. Again, by oxidation of another specimen, he can destroy the specific factor, so that it alone will fail to produce a tumor. When, however, he recombines the two specimens—the one in which the virus was destroyed, and the other, in which the chemical factor was destroyedand injects a small amount of this combination into a fowl, a typical Rous sarcoma will be reproduced. In other words, he brings experimental evidence that one factor alone does not produce a tumor, but that it is necessary to have the combination of both to reproduce the original type of tumor. My own experiments, reported about a year ago, confirm the production of Mouse Sarcoma 37 from a filtrate obtained from an anaerobic culture fluid, in which Mouse Sarcoma 37 was incubated for twenty-four hours.

Time does not permit me to dwell any longer upon this subject, but I would like to say a few words concerning the lead treatment of cancer. At the end of my paper I closed with a warning that we should be extremely conservative in the lead treatment. In the first place, it is dangerous, and because it is dangerous I feel that we ought not to use it in any but desperate, advanced. and non-surgical cases. I, for one, am not willing to treat early cases of cancer with lead until every other means is exhausted. I have treated a few of the advanced cases with lead, but so far with little result. That may not be the fault of colloidal lead: it may very well be my own shortcomings in technic. At present I am experimenting with lead in animals and obtaining more and more information every day. Personally, I do not feel that I want to experiment with different preparations of lead other than the colloidal solution Blair Bell is using, and I am perfectly satisfied to try it further and see what there is to it. Blair Bell makes use of very heroic doses; in other words, he administers four injections of 15 c.c. of colloidal lead at each injection in a one-half of 1 per cent solution over a period of from four to six weeks. he allows a month or six weeks to lapse and repeats the treatment with a second series. All in all, he attempts to get in anywhere from 600 to 800 milligrams of lead. Small doses of lead, in his experience, have not been satisfactory, whereas with the larger doses he seems to have more gratifying results. Another point to bear in mind is that the vascularity of the tumors has a great deal to do with the results; that is, the more vascular the tumor, the more gratifying will be the result. Scirrhous or fibrous tumors are very slightly affected. This holds true also in benign fibroids. So, too, the superficial epitheliomata are not favorably affected in particular. Once more let me emphasize that before lead treatment is attempted in an advanced case, be sure of the function of the kidneys, study the blood chemistry, and try to ascertain whether there are any metastases in the brain, lungs, or liver, for in these cases lead is contra-indicated.

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DR. SOILAND (closing): The discussion has had a very conservative trend, for which I am grateful. I am glad Dr. Quick found a note of optimism. [Laughter.] We attempted to sound a note of optimism, but really had very poor grounds to do so. I feel, however, that the knowledge that, for advanced cancer, we have no adequate treatment, means that surgery or radiation or both are inadequate to combat advanced cancer. Therefore, we are forced to use something which has an apparent scientific basis for its use, and when a man with the scientific status of Blair Bell, who has given six years of constant work to the study of this new form of therapy, and has really developed cases of advanced cancer that are cured, cases which some of us have seen with our own eyes-I repeat we must give this method respectful consideration. Further, we must use the lead exactly as Blair Bell lays it down. We have endeavored to do this according to his instructions, but we find that we cannot use the lead in the amount which he recommends without jeopardizing the life of the patient. Therefore, we are either not getting the kind of lead he uses or we do not know how to use that with which we are furnished. For these reasons we feel that we are justified in trying to modify the toxicity of the lead by the assistance of the best colloidal chemists available. we are hopeful of better results.

One of the gentlemen discussing this subject said something about the use of the beta rays of radiation. Now our thought is this: we know that the end-result of radium decay is lead: there is also really no difference between the action of the gamma rays of radium and the short wave X-rays. hence we assume that the same physiologic reaction occurs whether from the gamma rays of radium or the short X-rays, if used in approximately the same doses. that thought before us, we feel justified in placing within the tumor, if it can be done, an adequate amount of colloidal lead. If we can do this, we have the means of attacking the tumor from within by the lead and from without by radiation, and if either or both of these agents will destroy cancer cells, we believe that with the combination of these two agents we have a better weapon against this terrible disease, cancer.

As Dr. Sittenfield said, lead is dangerous; we called attention to that in our paper. As Dr. Ullmann said, you have to test the kidney function. We test the kidney, the liver, the blood and carefully supervise every patient on whom we use the lead. We would like to use the lead on earlier cases of cancer, but are a little hesitant to do so vet. We have so far used the lead only on patients who were beyond any other type of therapy. When we have become a little better acquainted with the action of lead, both by observation and personal experience, we may be able to use it in the earlier and more hopeful cases. Then we hope to state with a firmer conviction that there has been placed in our hands a more reliable agent than heretofore in our combat against that scourge of modern civilization, cancer.

Dr. Ullmann (closing): I want to discuss the question of optimism, for I believe our paper had a little more of it than that of Dr. Soiland.

In dealing with these hopeless cases of cancer, the type that we are treating with lead, one must hope that, even if this new

method is a failure, something of value may develop from it. If we could not keep that hope before us and a spirit of optimism, we could not stand the strain of caring for them very long: it would be too depressing. The determination of dosage relative to both patient and tumor is one of our pressing problems. It resolves itself into much the same problem as the dose of X-ray, the optimum dose, as I spoke of it several years ago-the dose that produces the maximum detrimental effect on the tumor and, at the same time, the minimum detrimental effect on the patient. Dr. Quick has suggested that the lead poisons the body as a whole and the tumor incidentally. We do not feel that this is quite true. Bell's idea is that it is somewhat specific and we can not see how it could poison the tumor as much as it does and at the same time leave the patient alive unless there was a certain degree of specificity. It is on this basis that we are working with the phosphate. The possibility of killing the patient in order to destroy the tumor is very much like the problem we had when we used the massive dose method with high voltage X-ray. In a paper attacking the use of the massive dose, I stated that a live patient with a stationary or regressing tumor was better than a dead one with a cured tumor. I believe that this applies to the use of lead as well as to the X-ray. In regard to reactions being due to the gelatin-that question was brought up in our laboratory. We always standardized its PH and we also noticed that the reaction apparently bore no relation to the preparation. Several patients would receive the same preparation at the same time and some would have a reaction while others would not. Dr. Quick spoke of the poor results they had observed in a few cases and the resulting pessimism. If one has the possibility of only 20 per cent beneficial results, as Bell states, that is only one out of five. One's first six or eight cases may all be

failures, but if one continues one may find a series showing good results, which will bring the average up. We have not found by autopsy any gross damage to the kidneys so far, and we have autopsied all but one of those patients who died-six. Dr. Quick asked why we should give lead and less Xray when a full dose of X-ray could be given instead. Our dose to the tumor is limited by the skin tolerance, so, if we can increase the susceptibility of the tumor to radiation by lead, we therefore increase the effect of the X-ray without damaging the I was much interested in the suggestion of Dr. Alvarez and hope such a method of testing patients can be developed. Dr. Bolliger spoke of their finding that glucose was toxic. We never made up the solution with glucose as the protective substance in place of gelatin, as Dr. Bolliger did, so have no data. Our solution contained gelatin as the protector and a small amount of glucose to prevent oxidation only. Our solution produced no more severe reaction than that prepared strictly according to Bell's method, neither was it more toxic to rabbits. The presence or absence of calcium seemed to have no effect on the reaction or toxicity. We have much more data than were given in our paper. Perhaps the suggestion made by Dr. Alvarez would be useful in preventing roentgen sickness. We might test a patient and then know how rapidly the dose could be given without producing sickness. We have had six deaths and five autopsies. One of these patients had been vomiting for twelve days and was almost moribund. She died four hours after the injection and I believe that this death might be attributed to the lead. The colloidal metal was used in this case. Two have died from a pneumonitis developing about lung metastases that were breaking down from the lead. We recognized the danger but gave the treatment

with full knowledge and consent of the patients, who were actually dying from their carcinomata.

I agree with Dr. Wallace that we should use radiation after the lead is given, be-

cause, if we radiate first, we will cut off a certain amount of the blood supply which will prevent the lead reaching the tumor and also because, after the administration of lead, the tumor is more radiosensitive.

Cancer of cervix.-The author calls attention to the reaction of the tissues to radium in the treatment of cancer of the cervix and the etiological importance of lacerations. At the Woman's Hospital in the State of New York, all patients treated with radium were encouraged to return for inspection once a month for five years or longer, and the reactions were found to be so nearly uniform that it was possible to predict the appearance of the cervix each month in cases progressing favorably. Five stages were noted: (1) a stage of hyperemia one week after the initial dose, the carcinoma and adjacent vaginal mucosa being intensely red and hyperemic; (2) three weeks later the cervix usually showed an extensive green slough, with foul discharge from the broken down carcinomatous tissue; (3) two months after irradiation the appearance was that of healing, the slough having separated, leaving a smooth, clean, dusky red cervix without any clinical signs of carcinoma; (4) a month later a stage of contraction caused by the development of connective tissue appeared; (5) the stage of marked contraction seen at subsequent examinations. Occasionally this shrinking of the cervix tightly closes the internal os and is accompanied by abdominal pain and signs of sepsis, which can be immediately relieved by dilatation and the discharge of purulent or bloody fluid. This may have to be repeated in women of the menstruating age.

From a study of 300 consecutive histories of cancer of the cervix repeated traumatizations of the cervix by labor or miscarriage appear to exert an important influence upon the occurrence of carcinoma. Careful palpation and visual inspection of every cervix immediately after confinement is advised, with the performance of trachelorrhaphy as a means of lessening the danger of cancer development, and, where this is contra-indicated, secondary repair should be effected later.

The Reaction of the Tissues to Radium in Treatment of Cancer of the Cervix and the Importance of Lacerations in Producing Cancer in this Location. Lilian K. P. Farrar. Surg., Gynec. and Obst., December, 1926, p. 719. (Reprinted by permission from Brit. Med. Jour., Jan. 22, 1927, p. 17 of Epitome of Current Medical Literature.)

A RHINOLOGICAL ASPECT OF BRONCHIAL ASTHMA¹

By W. V. MULLIN, M.D., Cleveland Clinic, CLEVELAND, OHIO

HEN your Committee invited me to present a paper on "the influence of diseases of the nose and of the paranasal sinuses upon the lower respiratory tract," they requested me to deal chiefly with that annoying and little understood symptom, bronchial asthma.

Abnormal conditions of the nose and its accessory sinuses may be factors in the production of three cardinal affections referable to the lower respiratory tract: (1) cough, (2) chronic bronchitis and bronchiectasis, and (3) bronchial asthma.

Cough.—In considering the production of a cough of nasal origin the individual hypersensitiveness of the nasal mucosa must be continually borne in mind. When one recalls that sensitive condition known as a "nasal tickle" it is easy to appreciate the effect upon a sensitive nasal mucosa of thermal changes and of chemical or mechanical irritants such as vapors and dust, and, in turn, to understand the effect of these stimuli upon the various reflex acts associated with the vasomotor and the sympathetic nervous systems.

The effect of a foreign body upon some noses—note that I say some noses, not every nose—makes it easy to appreciate the result of such frequently encountered mechanical obstructions as deviations of the septum, or the presence of spurs, of pressure, or of an hypertrophy of the turbinate, any of which may be aggravated by severe and repeated infections. Cysts within the sinuses—in the maxillary sinus in particular—often cause a cough; indeed, they are more likely to provoke a cough than is a purulent condition, and cysts within the turbinated bodies are also often responsible for an aggravating cough.

In an attempt to discover the effect of

nasal obstruction, Anderson (1) performed a number of experiments in which he plugged the noses of rabbits and dogs, the results of the experiments on the dogs being the most convincing. He attempted to close the nostrils of the dogs by sewing them together, but he was unable to keep both nostrils entirely closed. Nevertheless. as a result of this partial block the dogs developed a cough and asthmatic symptoms: they showed trophic disturbances such as dryness and wrinkling of the skin, and falling out of the hair, and at postmortem emphysema was found to be present. Of still greater significance than the above results, puppies born of mothers whose nostrils had been closed during pregnancy had markedly lowered resistance. Although the puppies received abundant food they failed to gain in weight and some of them died soon after birth, while those that lived were very susceptible to infection. These same disturbances, especially cough and asthmatic symptoms, are often seen clinically in cases of nasal obstruction.

Chronic Bronchitis and Bronchiectasis.— The relation of the nose and of the paranasal sinuses to the development of chronic bronchitis and bronchiectasis has been fully discussed in several other publications (2), to which very little can be added. Since I first reported in 1918-1919 that the presence of disease in the nasal accessory sinuses is an etiological factor in the production of bronchiectasis, this association has been proved, both by myself and others in hundreds of cases, and it is with extreme gratification that I read roentgenological reports such as the following: "The condition of this chest is suggestive of infection in the upper respiratory tract and disease in the accessory sinuses should be excluded."

Bronchial Asthma.—In discussing the relation of the nose and paranasal sinuses to

¹Presented before the Radiological Society of North America, at Milwaukee, Nov. 29-Dec. 4, 1926.

the production of bronchial asthma, it should be emphasized that asthma is a symptom and not in itself a distinct diseaseentity, as the latter conception is not only erroneous, but blocks the path to such a study of each case as alone will indicate the necessary measures for relief. This symptom must be classified before it can be properly discussed. According to the three primary causes therefor, cases of bronchial asthma may be classified as follows: (1) those due to sensitization to pollen, food, and other proteins; (2) those due to infection in the paranasal sinuses, and (3) those due to reflex stimulation. It should be understood that in any individual case a combination of these causes may be responsible.

Since I understand that the effect of sensitization to proteins is to be discussed by others on this program, I shall not offer any discussion of this factor in the etiology of asthma.

Allergy can cause asthma, even when no nasal disease is present. In cases in which asthma is associated with hav-fever, the asthma seldom develops until the hay-fever has persisted for several seasons, or, in some cases, the hay-fever is severe during the "hay-fever season," and the asthma appears in the Fall after the hay-fever has disappeared. It would appear that this might be explained on the premises that the havfever leaves the mucous membrane of the nose hypersensitive, that irritation has been caused by the long-continued pressure and closure of the nostrils, and that often a secondary infection is present, all these factors exciting a reflex which may be stimulated by atmospheric changes, by hot or cold air, by house-dust, or by any other irritant.

Infection of the Paranasal Sinuses.— Some authors advance the theory that sensitization to a bacterial protein is the cause of bronchial asthma in those cases in which it is secondary to sinus infection, but I have never been satisfied that this of itself alone is a sufficient explanation. The strictly

purulent type of sinus infection seldom causes asthma, but the hyperplastic type, which undergoes myxomatous changes and produces a luxuriant growth of polyps, causes asthmatic symptoms in a large percentage of cases. An infection of the tonsils or around the teeth is much less likely to cause asthma than are certain types of infection in the ethmoid or maxillary sinuses. It is certain that patients with certain types of hyperplastic disease of the sinuses, with recurring polyps in which the blood has a high eosinophile content and the polyps themselves contain eosinophiles, are especially sensitive to foreign proteins and to bacterial toxins. Cases of asthma in which the nose is blocked with polyps and the symptoms disappear after their removal, only to reappear when the polyps recur, occur far too frequently for one even to infer that the nose does not play an important part in the production of asthma. The maxillary sinus in particular may contain a low grade, dormant infection which is subject to periodic exacerbations. I have watched the changes which occur in these cases of sinus infection with the changing seasons and with changes in the weather. These patients may appear to be entirely well and are certainly free from all symptoms during the summer months, but with the return of cold weather the infection again becomes active, and when I have operated upon them I have found the sinuses to be so diseased that it was obvious that they had been infected for a long time.

Reflex Stimulation.—Very little is as yet known regarding the relation of reflex stimulation to bronchial asthma, but that such a relation exists, I am positive. I recall the case of a physician who had bronchial asthma and an infection of the maxillary sinus, in which a paroxysm would be produced by touching the external auditory canal with a cotton swab, the spasm being relieved by cocainization of the nose. The relief which asthmatic patients secure by the

use of the Tucker atomizer is undoubtedly due to the suppression of reflex stimulation.

Brodie and Dixon (3) have shown by experiments on animals that a bronchial spasm can be produced by stimulating the nose with a weak galvanic current, this undoubtedly being due to the fact, also shown by them, that the constrictor and dilator fibers of the muscular walls of the bronchi have their origin in the vagus nerve. Francis (4) has relieved asthma by applying the galvanic cautery to the nasal septum.

In this connection the following quotation from Sluder (5) is of interest: "The sympathetic nervous system in the nose is derived from the nasal ganglion. This receives its sympathetic nerve supply from the vidian nerve, the great deep petrosal, the carotid plexus and the superior cervical ganglion. Impulses may be transmitted from the inflamed nose by way of the nasal ganglion, the vidian nerve, the carotid plexus to the sympathetic trunk in the neck to the lower cervical and first thoracic ganglions."

For myself, I believe that the reflex stimulation that produces asthma must be due to pressure and obstruction in the nose or in the sinuses. On the other hand, the nasopharynx may be blocked with adenoid tissue; the oropharynx may be blocked with faucial tonsils; the larynx may be obstructed by a web or by a tumor; the trachea may be compressed by an intrathoracic goiter, and a stridor or a wheeze may result, but paroxysmal bronchial asthma will not be produced.

Diagnosis and Treatment.—It is obvious from the above discussion that if the treatment of asthma is to be successful, each of the many etiological factors which may be involved must be borne in mind. A tendency to allergy, a sensitive nasal mucosa subject to manifold reflexes, or hyperplastic disease of the sinuses, may be hereditary. The allergist who treats bronchial asthma without considering the possi-

bility that the nose and the sinuses may be diseased, or the rhinologist who does not consider the possible presence of allergy, will alike meet with failure.

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CASE HISTORIES

The following two case histories are offered as illustrating well the relation of bronchial asthma to affection of the paranasal sinuses, and the possibility of relief by radical operation.

Case 1 (173,454). A man, 32 years of age, came to the Clinic because of repeated attacks of shortness of breath and of coughing, with the expectoration of considerable sputum but no blood. He stated that he became short of breath whenever the weather was damp. During the preceding four days he had had "shortness of breath" both during the day and the night.

Nose and throat examination showed a septum deviated to the right, with an anterior perforation and crusting in both nares. The tonsils were large, cryptic, and filled with definitely infected material. The Wassermann reaction was negative.

X-ray examination of the chest gave negative findings, but an X-ray examination of the sinuses revealed the presence of pus or granulations in both antra, the other sinuses being normal.

The complete removal of the tonsils and of all the infected areas in the sinuses was recommended and about a week later the patient entered the hospital for operation. At that time the asthmatic symptoms were marked. The right maxillary sinus was opened through the canine fossa. The antrum was found to contain thick, creamy, purulent material and polyps. The entire lining of the right antrum was diseased and was therefore removed. A similar operation was performed on the left antrum, which was not as diseased as was the right, contained no purulent material, but did contain some polyps, which were removed. The

culture showed that hemolytic streptococci had been present on both sides.

Pathological diagnosis: Chronic inflammation; cysts of the antra of Highmore.

The patient made a good recovery and has not had any attacks of asthma since the operation.

Case 2 (166,929). A man, 35 years of age, came to the Clinic complaining of attacks of paroxysmal asthma which occurred principally at night. He stated that one older brother and one sister had both suffered from asthma. Tonsillectomy and adenoidectomy had been performed in the preceding year. Five months before he had driven twenty miles in an open car in belowzero weather and had taken a severe cold. as a result of which he began to cough and to have attacks of wheezing at night. Pain developed over the right side of his face and there was a discharge from the right nostril. He consulted a physician, who irrigated the right maxillary sinus, as a result of which the patient was somewhat relieved. He had had these irrigations seven times, but the last two times they had been followed by an exacerbation of the asthma.

An X-ray examination showed the right antrum to be suspiciously clouded. The other sinuses and the chest were clear.

The patient entered the hospital and the right maxillary sinus was opened through the canine fossa. The antrum, which was large, was found to be completely filled with pyogenic purulent material, the entire lining being diseased and polypoid. Culture showed the presence of staphylococci. This patient made a good recovery and remained free from asthma until late in the Summer, when, as the result of a cold, he had an attack of asthma.

The following case illustrates the relation of asthma to paranasal infection and allergy. Case 3 (169,751). A woman, 27 years of age, came to the Clinic complaining of having had a sore throat for a week, of a

cough, and of inability to breathe through her nose. She stated that when she was twenty years of age she had had what she thought was hay-fever, which was accompanied by some asthmatic symptoms. At that time, polyps were removed from both nares, with resultant relief from the symptoms. She had had no further trouble until the time of this visit to the Clinic.

On examination the nose was found to contain thick mucoid material. The voice sounds were muffled and obstructed. Polyps and hyperplastic tissue were present in both middle meati.

An X-ray examination showed the presence of pus or granulations in the right antrum and in the right frontal and the right ethmoidal sinuses. The other sinuses were normal.

Local treatment was applied and the patient was told to return for further treatment and examination.

A week later she came back with a marked cough and asthmatic wheezing and was sent to the hospital for operation. The right antrum was opened through the right canine fossa and several infected polyps, together with the mucous lining of the antrum, were removed. Bilateral ethmoid operation done.

Pathological report: Walls of polyps very edematous; sac composed of a single-cell layer of columnar epithelium. Large number of leukocytes, mainly lymphocytes, plasma cells and eosinophiles. Culture from right antrum showed streptococci, pneumococci, and diphtheroid bacilli.

The patient recovered almost immediately from her cough and began to gain in weight. She had no more attacks of asthma until three weeks after her operation, when she spent one night in the country and had an attack of asthma after going to bed. She found that she was sleeping on a feather bed. This was removed, the asthma disappeared, and she had no more attacks.

The interesting feature in this case is the

primary relation of the attacks of asthma to the infected sinuses and to allergy.

The following case illustrates the relation of a reflex cough to a sinus affection.

Case 4 (169,737). A woman, 29 years of age, came to the Clinic because of severe paroxysms of coughing unaccompanied by sputum. She gave no history of fever or She had gone to another of sweating. climate without securing any relief. Five years before she had had a cold which had left her with some nasal trouble and a catarrhal discharge from the nose; she suffered also from headaches at the time. Her tonsils had been removed, also a part of one middle turbinate, and a submucous resection had been done. She had not been relieved by these operations; on the contrary, her cough had increased.

A physical examination revealed nothing of importance.

An X-ray examination showed the presence of pus or granulations in the right antrum, the other sinuses being normal in appearance. X-ray examination of the chest gave the appearance of a recent influenzal infection in the right upper lobe, although the possibility of an early pulmonary tuberculous condition could not be definitely ruled out.

The patient entered the hospital for opperation. The right maxillary sinus was opened and disclosed a large cyst which almost filled the sinus.

Pathological diagnosis: Chronic inflammation; multilocular cyst.

The patient's condition improved at once. She gained in weight and the cough disappeared.

In this case the cough was obviously reflex in character, being due to reflex stimulation by the maxillary cyst.

Discussion.—The diagnosis of sinus-chest condition requires even more than co-operation among the roentgenologist, the internist and the rhinologist; it requires an intimate and thorough understanding on the part of each of the language of the others—strange tongues make for overlooked or mistaken diagnoses. Roentgenograms which are properly taken and properly interpreted are indispensable. I have opened many antra in cases of bronchial asthma and have found them filled with polyps, of the presence of which I had no other evidence—except for a carefully taken history—than a dense opacity shown by the X-ray, and I defy any rhinologist to make this diagnosis without an X-ray examination.

It must be remembered that a polyp or hyperplastic tissue cannot be washed from a sinus.

The possibility that bronchiectasis may be present should not be overlooked, for there is nothing constant or characteristic about the chest-picture in asthma; but since lipiodol has come into use, the diagnosis of bronchiectasis has become very much simplified.

The rhinologist has ofttimes been accused, and often justly, of performing unnecessary nasal operations in such cases as we have The term "justly accused" is described. used because of the fact that the minor operations which are too frequently employed are of little or no avail. Neither the removal of the middle nor inferior turbinates, nor the opening of a few of the ethmoid cells will produce permanent results, and the same may be said of the partial removal of polyps. Every vestige of the diseased tissue must be removed. This cannot always be accomplished by intranasal surgery. I make no plea for the routine employment of radical procedures, but in a case of bronchial asthma in which hyperplastic disease affects all the sinuses, and the morphology of the sinuses has been well studied by means of a good X-ray plate, my judgment would be either to eradicate all infection or to let it alone.

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Chronic sinusitis.—The author advocates the use of iodized oil as an opaque medium in the radiological diagnosis of chronic sinusitis and maxillary cysts. A thorough irrigation of the antrum or frontal and sphenoidal sinuses with sterile saline solution is first performed, to wash out any free pus. The solution is carefully removed and 5 c.cm. of 10 per cent iodipin is injected, a stereoscopic X-ray view being taken as soon as possible afterwards. MacCready states that, though the ethmoid sinuses cannot be injected, much can be learned from the course of the iodized oil as it passes into the nasopharvnx, since normally the cilia carry it back in definite currents.

In chronic sinusitis thickening of the mucous membrane, with the frequent formation of small abscesses or a polypoid degeneration, results, and this thickening of the lining membrane of the sinuses is readily demonstrated by X-rays after injection of iodized oil. obscure cases where changes have been produced long after all sinus symptoms have subsided, this method, by demonstrating a thickening only amenable to operation, may save the patient the discomfort of those useless repeated irrigations which in the absence of X-ray diagnosis are usually employed before surgical intervention.

The author adds that the treatment of chronic frontal sinusitis differs from that for chronic antrum infection because many frontal sinus cases clear up with the establishment of drainage. Iodized oil should be reserved for those which do not so respond. The oil is removed from the sinuses too rapidly to be of much use therapeutically, and while the removal from the antrum may take twenty-four hours, it is much quicker from the frontal sinus. Little discomfort follows the injection. though there may be a feeling of congestion in the cervical glands owing to a small amount of the oil being absorbed by the lymphatics.

Iodized Oil as an Aid in the Diagnosis of Chronic Sinusitis and of Maxillary Cysts. Paul B. MacCready. Boston Med. and Surg. Jour., Sept. 2, 1926, p. 464. (Reprinted by permission from Brit. Med. Jour., Oct. 30, 1926, p. 67 of Epitome of Current Medical Literature.)

THE DIAGNOSTIC VALUE OF IODIZED OIL IN INTRA-THORACIC LESIONS¹

By ADOLPH HARTUNG, M.D., CHICAGO

ODIZED oil owes its value as a diagnostic aid in roentgenology to the facts that it is radio-opaque, non-irritating, and practically harmless even when retained for long periods of time. It lends itself readily to the requirements of a contrast medium in intra-thoracic lesions because of its fluidity, and the technic of its application is comparatively simple and easily mastered. Although it is especially suitable for intratracheal administration, its use for local injection through fistulous openings has advantages over other substances formerly used for this purpose. The information to be derived from its use depends primarily upon its entry into and distention of hollow spaces, a rather self-evident fact which deserves to be emphasized because it indicates in a general way its range of usefulness and limitations.

The roentgen image presented by the oil in lungs of normal cases shortly after intratracheal injection bears a striking resemblance to a tree minus its leaves. The trachea and larger bronchi are usually outlined by oil adhering to their walls, whereas the lumen of the smaller bronchi are irregularly filled with it. In the parenchyma an intertwining network with coarse stippling is shown. If an insufficient quantity of oil has reached the part, there may be an abrupt termination of the shadows simulating an obstruction; an excessive amount produces so much overlapping of superimposed shadows as to obliterate all detail.

A considerable portion of the injected oil is coughed up ten or fifteen minutes after its administration and at intervals thereafter. The remainder is absorbed very gradually. Residues have been observed for more than three months in some of our cases. Prolonged retention was noted far more frequently in normal areas than in bronchiectatic ones. Retained residues gradually give the lung a coarsely mottled appearance strongly resembling soft infiltrations. These may lead to faulty interpretations on subsequent roentgen examinations made without knowledge of the previous history.

Pathologic conditions demonstrable by the injection of iodized oil manifest themselves either by changes in the size, shape or position of normal tubular structures or by indicating abnormal channel formations or cavities.

The need for additional information such as can be furnished by the use of a contrast agent has undoubtedly impressed itself upon every one who has endeavored to interpret doubtful shadows presented on many roentgenograms or tried to reconcile apparently negative roentgen findings with definite clinical evidence of pulmonary pathology. The lesions may be so located or the pathologic changes be such that they cannot be demonstrated by the ordinary examination. Oftentimes the exact location or extent of the condition cannot be judged even when its presence is indicated. Secondary changes in the surrounding structures may obscure the nature of the primary pathologic processes to such an extent that these can be determined only with the aid of a contrast medium.

The conditions in which the use of iodized oil has proven itself of value are: (1) Bronchiectasis; (2) lung abscess; (3) chronic suppurative processes in the lung; (4) intra-thoracic neoplasms; (5) foreign bodies; (6) pulmonary tuberculosis; (7) chronic empyema; (8) fistulæ of the chest

¹Read before the Radiological Society of North America, at Milwaukee, Nov. 29-Dec. 4, 1926.

wall. The information to be derived from it is of value not only in a diagnostic way but often influences the prognosis and treatment. It assists the thoracic surgeon in the selection of cases suited for surgery, the type of operation indicated in the individual case, and often shows him the need for additional operative procedures when symptoms persist after the original operation.

"Pneumonography" or bronchography, as introduced by Forestier and Sicard, has thus far found its greatest field of usefulness in bronchiectasis. In this condition the dilatations are demonstrable with its aid even before chronic infections in them have produced sufficient fibrosis to render them visible roentgenographically or before the clinical picture is characteristic. They may be shown when located behind the heart or overshadowed by part of the diaphragm where they might thus escape detection on the simple roentgen examination. shape, size, and extent may be accurately determined, which knowledge is of great importance in deciding upon the best method of treatment. Information may be obtained as to whether the condition is uni- or bilateral, a consideration which enters largely into the case when operation is contemplated. By making early diagnosis possible, especially in children, it may lead to cure by conservative measures and prevent the late manifestations which are usually resistant to all but radical means.

In lung abscesses, the method has not given the assistance hoped for—at least not in the recent cases. The pneumonitis surrounding the abscess or debris in it usually prevents the oil from entering. In chronic cases, where the nature of the pathologic processes present is largely masked both roentgenographically and clinically by the fibrosis present, bronchography may give much valuable information. It may show the presence of one or more abscess cavities and their relation to the larger bronchi,

thus indicating whether bronchoscopic or surgical drainage offers the best method of treatment. It may show a honeycombing of the area by irregular channels, suggesting cauterization as a preferable procedure. Where symptoms persist after operation, injection of the iodized oil may show a complicating bronchiectasis, which has been found to be a not infrequent accompaniment.

In chronic suppurative processes of the lung the conditions are much the same as in isolated abscesses except that the changes are more extensive and therefore much more obscure. In these, frequently all lung details are absent on the ordinary roent-genogram and the use of a contrast agent is absolutely essential to show if a lung cavity be present.

Valuable information relative to intrathoracic neoplasms may occasionally be obtained by bronchography. The origin of the tumor may be indicated by obstructive phenomena or deviations of the trachea or bronchi.

Bronchography may serve to localize a foreign body in the chest relative to the bronchi. Doubtful shadows suspected of being aspirated foreign bodies may at times be differentiated from calcified nodules with its aid, as in a case reported by Clerf (1). Pritchard, Whyte, and Gordon (2) reported a case of abscess secondary to a foreign body, discovered with its aid, which was not demonstrable otherwise.

In pulmonary tuberculosis, the use of iodized oil injection is of doubtful value save in exceptional instances. Rapidly progressive types of the disease, febrile cases, and those with recent hemoptysis are generally regarded as unsuitable. In the few cases in which we have used it, no harmful results have been noted and very few have been recorded in the literature. One finding repeatedly seen when any bronchiectatic dilatations were present was that these were

rather nodular in character. Cavitation, although demonstrable by this method, hardly warrants its use because, even if operation is contemplated, its purpose is to collapse the cavities rather than to drain them. After operation, the persistence of symptoms may indicate the need for bronchography to determine if the cavities have been obliterated. Archibald (3) reports three cases illustrating its value under these circumstances. The method may be of value in demonstrating lung tissue in adhesions resisting collapse after pneumothorax treatment, thus contraindicating cauterization. Annular shadows may at times be differentiated from cavities by lack of filling after injection.

Chronic empyema produces a variety of pathologic changes which are practically impossible of accurate interpretation on the roentgenogram in the great majority of cases without the aid of a contrast agent. Here iodized oil has proven itself especially valuable in localizing cavities, showing their size and possible communicating channels. Fistulous tracts can likewise be followed with it through the various ramifications to the source of origin. Bronchopulmonary fistulæ may thus be demonstrated and causes for persistent sinuses be disclosed.

In determining the diagnostic value of iodized oil in intra-thoracic lesions, consideration of its harmlessness is of primary importance. Forestier and Sicard demonstrated this by experiments on animals before applying it in the case of humans. Untoward results from bronchography recorded in the literature are practically negligible. Of the cases examined by this method in our clinic none seemed to be the worse for it. Most of the patients had both sides examined at different times and in some of them it was repeated. Several were out-patients who went home shortly after the procedure. In none of them was their usual cough exaggerated-in fact, some seemed improved after it. No febrile flare-ups nor

late complications such as abscess, bronchiectasis, nor fibrosis have been noted. Prolonged retention seems to exert no deleterious influence.

The second consideration is the reliability of the findings obtained with it. All who have used it agree that positive information derived from it has definite diagnostic value. Negative findings do not necessarily indicate an absence of pathology. Sergent and Cottenot (4) especially have stressed this latter point. When it is recalled that 15 to 30 c.c. of oil is injected into spaces capable of holding several liters of air, the possibility of its failure to reach affected parts is readily apparent. Secretions in the bronchi, stenosis, or compression of them may obstruct the passage of oil into distal parts and lead to faulty interpretations. Since gravity is largely relied upon to guide the oil into the desired parts in all but the bronchoscopic method of administration, errors may result from faulty posturing. Functional or organic disturbances affecting respiration may influence the aspiration factor of distribution.

CONCLUSIONS

A review of the literature and our own experience seem to justify the following conclusions:

- Iodized oil is an ideal contrast medium for use as an aid to roentgenologic diagnosis in intra-thoracic lesions.
- 2. Its need is based on the fact that the roentgen and clinical findings in many cases give no adequate information of the pathologic processes present without it.
- 3. The indications for its use are varied and numerous. From the roentgen standpoint all conditions in which information may be obtained by distending natural or acquired hollow areas may be advantageously investigated with it. From the clinical standpoint, cases in which the history, physical findings, laboratory, and ordinary roent-

gen examinations do not give an adequate diagnosis, should be subjected to it.

4. Positive findings obtained with it have definite diagnostic value.

Before closing, I should like to express my appreciation and thanks to Dr. Hedblom and Dr. Head for permission to utilize the information which their cases and work made available for the roentgen study upon which this paper is largely based.

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DISCUSSION

Dr. Jerome R. Head (Chicago): I have very little to add to Dr. Hartung's excellent discussion of the diagnostic value of iodized oil in intrathoracic lesions. He has covered the field very completely and thoroughly. I would, however, like to say a few things about four different aspects of the subject: (1) The future of the method; (2) its particular value in the field of thoracic surgery; (3) the question of its innocuousness, and (4) the technic of injection.

Whoever has used the method must, I am sure, feel certain that it is a great advance in the diagnosis of thoracic disease, that it has come to stay, and that in certain types of cases where the indications are present it will become as routine a procedure as pyelography or the opaque meal in gastro-enter-The method is still very new: although it has been in use five years it is only now being generally adopted. There must, consequently, be much that we have still to learn from it. There is no doubt but that in time we will be able to make more intelligent interpretations of the plates and come to recognize minute changes which, so far, have escaped observation. It should help greatly in the investigation of the physiology of the bronchial tree. Already it has taught us that the respiratory mucous membranes are much more tolerant of foreign materials than anyone has believed heretofore. It has shown us that cough scatters material from one part of the lung to all the other parts, and that while evacuation of material from the larger bronchi and from bronchiectatic cavities is rapid, that lodged in the finer air spaces of the normal lung remains in place for weeks and months.

To the thoracic surgeon the method has been of particular value. Most of his patients come late and are the victims of longstanding suppuration. The physical findings and the roentgenograms are consequently often obscured by fluid, pleural thickening, or parenchymal fibrosis and pneumonitis. Where, before, he has worked on inference and exploration, he can now obtain before-hand a clear visualization of the pathology. In bronchiectasis the ordinary roentgenograms frequently show little or nothing. One is confronted by a patient who is raising quantities of sputum yet whose physical and X-ray examinations give but slight information as to its source. It is in this type of case that lipiodol has proven most valuable. It will probably show us that many cases with atypical symptoms, heretofore classed as chronic bronchitis, are, in reality, instances of early bronchiectasis. By making possible an early diagnosis it will give the patients the advantages of early treatment.

In regard to the effect of the oil upon the bronchi and lungs, one can only say that so far no accidents or untoward results have been observed. It has been in use five years and many thousands of injections have been performed.

We have used all of the different methods of injection—the supraglottic, the transglottic, the passive method of Alton Ochsner, and the direct puncture of the trachea through the cricothyroid membrane. Our most extensive experience has been with the latter. We vary the method of injection with the indications of the particular case. We agree with Forestier that the direct puncture method is the simplest, the most certain, and the most universally applicable. It is not dangerous and it is not more painful or more disagreeable than the other methods.

DR. KENNON DUNHAM (Cincinnati): May I have Dr. Hartung's last slide put on again? I wish there was more time to discuss all of these papers-they are most interesting. If you will study the trunks which the lipiodol brings out, you will have no trouble in getting the anatomy of the lungs as so beautifully shown by some of The tree of the bronchus is the plates. wonderfully brought out. A study of the anatomy so shown is essential in studying any lung condition. You have in this method a means of studying your lobation by the trunks to the various lobes.

In this last plate in which the Doctor called attention to an annular shadow, I think you will have a great chance to study these trunks. I cannot say from this flat plate exactly what would be seen if it was studied stereoscopically, but I have an idea that it is a cavity. I am perfectly sure that this is not an annular shadow, but a cavity, although I can not prove it. It is a most serious condition; a condition which you X-ray men can and must diagnose. That girl's life depends upon pneumothorax or thoracoplasty; the collapse of that lung

closes that cavity. You have a large cavity in the upper third of your lower lobe. Now that is the most dangerous place to have a pulmonary cavity, due to tuberculosis. This is why I have been fighting so many years against the casual diagnosis of annular shadows. When that cavity was brought out on the screen a while ago. I felt that it was absolutely essential that you men should go home and take up this study. The fact that the lipiodol did not fill that particular area does not disprove the presence of cavity. Tuberculous cavities seldom ever fill, and while some of them may be open. many are not. That is the study of the trunks going to the upper third of the lower lobe, which will prove or disprove my contention. If the trunks in this case, as shown by the stereoscopic plates, were seen to go to the upper third of the lower lobe, then you would have a perfect right to say that this is not a cavity, but just because it did not fill with lipiodol permits no such conclu-You are the only people on God's green earth who can accurately diagnose such a lesion, and I think that is a responsibility you must assume. Physical signs will not show a cavity there. That is a good plate: I could not help stopping long enough to speak about it.

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DR. HARTUNG (closing): In regard to Dr. Dunham's discussion relative to this annular shadow, I remarked in my paper that it is possible to have cavities and not be able to fill them. In this particular case it seems quite logical to expect the lipiodol to flow into the cavity, as it is apparently empty, if there is a connection with the bronchus. That, of course, is the one thing that it is necessary to get definite information about. We have no filling of this annular shadow, so presumably the area is not connected with a bronchus and we may infer that there is none, equally as well as the Doctor may infer that there is a cavity. Clinically,

I believe this patient did not have a condition which would warrant the drawing of the conclusion that this was a cavity. I have a slide of a tuberculous cavity shown by means of lipiodol injection in a youngster who had been treated by pneumothorax treatment. A roentgen examination showed a large area of radiolucency and the question of a cavity came up. In this particular case the lipiodol flowed into this area and then spread on either side of the bronchial opening into it; turning the patient upside down, it was possible to get the lipiodol into

the upper region of this particular rarefied area, and the conclusion was drawn that it was a localized pneumothorax with a fistulous connection with the bronchus. In the former case I do not believe there was a cavity. I think this was an annular shadow.

In conclusion, I would like to suggest the general use of a term such as "pneumography" or "bronchography" for the procedure of injecting lipiodol into bronchi, just as we use the term "pyelography" for the injection of opaque media into the urinary tract.

Acid base equilibrium after irradiation.—
This is a brief report of the extensive investigations undertaken to study the changes in the acid base equilibrium of the organism (rabbits and human beings) following roentgen-ray exposure. The urine did not show any appreciable fluctuation in the hydrogen-ion concentration. The reaction of the blood appeared in two phases; directly after the treatment there was a slight acidosis which turned into alkalosis two to five hours later. The degree depended upon the part exposed; an increasing scale from extremities, ovaries and uterus, thorax and abdomen was noted. The

first phase is believed to be due to a direct roentgen effect, the second phase may have its cause in a stimulation of the vagus by the products of decomposed albumins. All patients with liver disease had a definitely reduced alkali reserve. The treatment of these cases by roentgen rays or the administration of a general anesthetic (ether or chloroform) is, therefore, dangerous.

E. A. Pohle, M.D.

The Influence of Roentgen Rays on the Acid Base Equilibrium. G. von Pannewitz. Strahlentherapie, 1926, XXIV, 327.

IODIZED OIL AND PNEUMOPERITONEUM IN GYNECOLOGY¹

A CLINICAL RADIOLOGICAL STUDY

By IRVING F. STEIN, M.D., and ROBERT A. ARENS, M.D., Departments of Gynecology and Radiology, Michael Reese Hospital, CHICAGO, ILLINOIS

practical utilization of pneumoperitoneum and its application to gynecology. Forestier at that time exhibited films illustrative of the use of an iodized oil in the diagnosis of uterine and tubal disorders. It occurred to us that, while the latter was a very valuable addition to our armamentarium, the combination of the two methods, pneumoperitoneum and transuterine iodized oil instillation, would undoubtedly be of more value than either alone. In the past year, we therefore made a number of observations utilizing this combined method. We desire now to demonstrate the results thus obtained and shall attempt to evaluate the combined method in terms of the other two separately. None of these methods has been used routinely by us in the diagnosis of our gynecologic material, but only in those cases in which the diagnosis was incomplete or unsatisfactory by other clinical means.

The technic employed in this work is the same as described in our previous paper for the induction of pneumoperitoneum and the subsequent taking of films utilizing the Potter-Bucky diaphragm, the patient being in the partial knee-chest position following pneumoperitoneum. Before turning the patient over in this position, however, a bivalve vaginal speculum is introduced and a special cannula is inserted into the cervix, through which the iodized oil is instilled. To prevent the backflow of the contrast oil the cannula is fitted with a special olive-shaped rubber obturator through which the

AST year we demonstrated before the cannula passes. The olive is pressed firmly Radiological Society of North Ameragainst the external os and traction is made ica the results of our studies in the with a single vulsellum on the anterior lip.

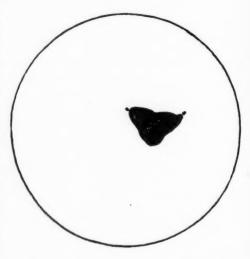


Fig. 1. Lipiodol instillation. Apparent obstruction of fallopian tubes at uterine cornua.

This latter procedure can also be done after the patient has been placed in the knee-chest posture so that the iodized oil is instilled just before arranging the patient on the Bucky diaphragm. Only sufficient pressure is used during instillation to fill the uterine cavity and fallopian tubes. It is extremely difficult to gauge the amount of pressure needed, especially when using too small a syringe, or one with too small an opening, and for the purpose of obviating this difficulty we have employed a special glass syringe with an outlet large enough to permit of easy flow of the heavy oil (lipiodol).

With the use of the roentgen-opaque oil only a limited amount of information is ob-

¹From the Adolph Stein Memorial for Research in Roentgenology. Read before the Radiological Society of North America, at Milwaukee, Nov. 29-Dec. 4, 1926.

tainable, such as the visualization of the uterine cavity and fallopian tubes, when filled. If there is a point of obstruction in

omitted instrumentation or intra-uterine instillation, although Heuser has shown that by using iodized oil in such cases a typical

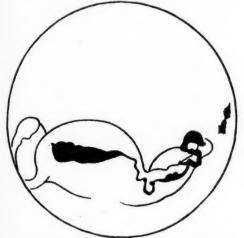


Fig. 2. Lipiodol instillation. One tube completely filled and proved patent by escape of the oil from the fimbriated end. Other tube apparently obstruct-Pneumoperitoneum reveals no pathology and both tubes found patent when tested at laparotomy.

the tubes, the iodized oil will pass only up to this point (Fig. 1). It is possible that one tube may be patent, this tube filling completely, the opaque media escaping from the fimbriated end, while the other tube will fail to show because of apparent occlusion. The information obtained, however, is limited, since one tube may offer less resistance than the other, in which event that tube is likely to fill first, and as the intra-uterine pressure is increased the opaque oil will pass entirely through this one tube but not through the other, even though the second tube may not be occluded, as in Figure 2. In this patient the transabdominal pneumoperitoneum failed to disclose any pathological condition on the side of apparent occlusion and at laparotomy both tubes were proven

In early pregnancy we have entirely

patent by the method of Curtis, air passing from the first tube through the uterus and

seen to escape from the fimbria of the op-

posite side.



Fig. 3. Transabdominal pneumoperitoneum. Pregnancy, two months (no iodized oil used).

defect in the contour of the uterine cavity may be of diagnostic value. We believe, however, that where roentgenographic aid is required for diagnosis or for verification of early pregnancy, transabdominal pneumoperitoneum will fill that need, and that instrumentation and transuterine instillation are contra-indicated. In the case illustrated in Figure 3, roentgenographic verification of early pregnancy in an unmarried girl was desired as a matter of legal evidence. The value and significance of a film for this purpose and the necessity of avoiding intra-uterine instrumentation can readily be appreciated. We would likewise hesitate to use any transuterine method in soft uterine growths for fear of interfering with early pregnancy, when the diagnosis is uncertain, as in the case of a large soft uterine fibroid simulating pregnancy (Fig. 4). In subacute and chronic inflammatory lesions transabdominal pneumoperitoneum yields the greatest amount of information with the least amount of trauma, and in selected cases may be combined with the use of the opaque oil. We are not convinced, however, that any oily substance is entirely harmless within the body cavities. Our pathologist, Dr. O. T. Schultz, reported to us a case of foreign body granulomata on the site of an old chronic salpingitis in which we had used lipiodol four months

Fig. 4. Transabdominal pneumoperitoneum. Large soft fibroid simulating pregnancy (no iodized oil used).

previously. Proof is incomplete, however, that the oil entered the tubes, as the films disclosed filling of the uterine cavity only. While Forestier mentions that the iodized oil is harmless in the tissues, we are reminded of the work of Laughlin in which mentholated albolene dropped into the nasopharynx in infants produced bronchopneumonia, and that he was able to reproduce the pathologic changes experimentally in animals.

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Pneumoperitoneum may show the extent of enlargement and displacement of pelvic viscera, as well as the relation of the surrounding structures to the pelvic contents. whereas, if intra-uterine instillation alone is used and the tubes are obstructed, only this latter information can be elicited; the uterine cavity and the tube lumen up to the first point of obstruction will thus be shown. When the obstruction is in the interstitial portion of the tube only the uterine cavity is outlined (Fig. 1). The latter method does not give any additional information as to the extent of tubo-ovarian involvement. or as to the presence of adhesions to the bowel, omentum, or peritoneum (Figs. 5

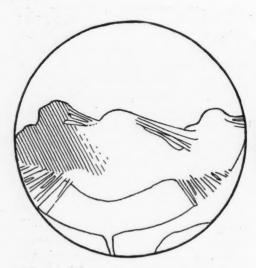


Fig. 5. Transabdominal pneumoperitoneum. "Frozen pelvis." (No iodized oil used.)

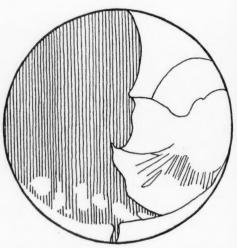


Fig. 6. Transabdominal pneumoperitoneum. Dense pelvic and abdominal adhesions (no iodized oil used).

and 6). When the tubal obstruction occurs at the fimbriated end, iodized oil alone may reveal the dilated, tortuous, distorted, or constricted lumen, but the extent of the pathology in the pelvis cannot be determined except by the additional use of transabdominal pneumoperitoneum. In the case illustrated in Figure 7, no abnormality was elicited on palpation, but in a patency test the tubes were found to be obstructed. Five

c.c. of iodized oil was then injected to disclose the point of obstruction and a transabdominal pneumoperitoneum was induced. Both tubes filled up to the fimbriated end, but at this point were obstructed; the right tube in addition was found to be considerably dilated and tortuous. The pelvis further contained two rather large globular



Fig. 7. (A) Combined lipiodol instillation and pneumoperitoneum. Both tubes obstructed at fimbriated ends. One tube dilated and tortuous. Cystic pelvic masses revealed by pneumoperitoneum.

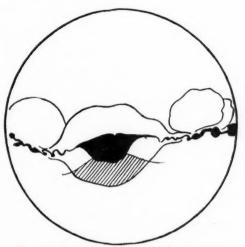


Fig. 8. (A) Combined lipiodol and pneumoperitoneum. Patent fallopian tubes. Apparent beading (peristalsis?) of tubes.

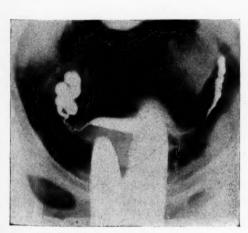


Fig. 7. (B) Roentgenogram of same.



Fig. 8. (B) Roentgenogram of same.

masses suggesting bilateral tubo-ovarian swellings, evidently containing fluid. At laparotomy these masses were found to be peritoneal serous cysts originating in old tubo-ovarian adhesions and surrounding the adnexa on both sides. Peritoneal inflammatory cysts of this type are usually not detected by palpation.

In the past few months a number of articles have appeared in American literature on the use of iodized oil in gynecological diagnosis. This renewed interest in the transuterine use of opaque substances was undoubtedly the result of Forestier's report. Among these are notably the contributions of Newell, Randall, and Rubin and Bendick, none of whom considered pneumoperitoneum in conjunction with the opaque method.

Apparent beading or tubercle-like nodes, described by Newell, are not due to tubercles, pathological dilations, strictures or diverticula of the tubes, but are due to crosssections of the convoluted tube lumen. Rubin and Bendick very recently reported having observed tubal peristalsis through the fluoroscope with the aid of lipiodol. Apparent peristalsis can be produced in almost any hollow viscus by distending it with fluid. This, however, is a defense reaction in an attempt to overcome undue distention. We have failed to observe peristalsis fluoroscopically in cases in which the iodized oil filled the tubes. The oil is visible through the fluoroscopic screen, but the tubal lumina are too fine to detect minute changes in contour. Beading, as seen on the film, was not observed.

The combination method is advantageous in outlining the course of the tubes, of showing dilatations, tortuosities, proving patency by the escape of roentgen-opaque oil through the fimbria, and clearly differentiating the tubes from the other pelvic viscera (Figs. 8 and 9). It is obvious then that more information can be obtained by

the methods combined than by either alone; the one—iodized oil instillation—disclosing the condition of the lumen of the uterus and tubes with irregularities, changes in lumen, obstruction, etc., while the other—

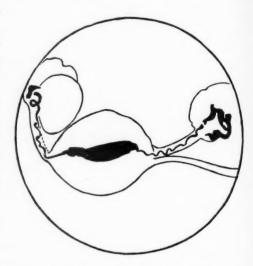


Fig. 9. Combined lipiodol and pneumoperitoneum. Patent fallopian tubes.

pneumoperitoneum—by outlining the pelvic viscera discloses any change in size, shape, and density, resulting from pathological processes. If one method alone were to be employed, we would elect pneumoperitoneum as our method of choice because of these factors, whereas with iodized oil alone the demonstration of existing pathology depends entirely upon the successful filling of the lumen or cavity of a hollow viscus, and discloses only the first point of obstruction, if one is present. Furthermore, thousands of recorded cases of pneumoperitoneum attest to its safety, whereas iodized oil is still on trial.

The diagnostic method to be employed in any given case should be governed by the pathology present as determined by the history and a clinical examination. We do not recommend the routine use of either method

alone or in combination, but urge a judicious and careful discrimination as to the method of choice when roentgen aid is sought. Even straight films may be indicated. In a recent case of parovarian cvst. liniodol instillation would probably have shown nothing diagnostic; whereas, by means of pneumoperitoneum, we were able to demonstrate a characteristic cyst outline in addition to both ovaries. In another case. a calcified fibroid, an ordinary film covering the area was sufficient to verify the clinical diagnosis, neither method being indicated.

The methods under discussion do not detract from the value of the Rubin patency test, so useful in sterility, but rather enhance its value by supplying additional information to that already obtained. When tubal obstruction is encountered in a patency test and a pressure of 200 mm. of mercury is maintained in two or three trials, the use of iodized oil will prove valuable in locating the point of obstruction. Occasionally the use of the liquid medium will prove tubes patent which seemed obstructed when tested with air or gas. When additional information is desired, such as the size of the uterus or ovaries, or the presence or absence of adhesions to the pelvic viscera or other pathological changes, pneumoperitoneum must be utilized.

CONCLUSIONS

1. Transuterine insufflation of CO2 is recognized as a safe and useful procedure in gynecologic diagnosis.

2. Diagnostic pneumoperitoneum stands as one of the most vivid and useful methods of projecting pelvic pathology on the roentgen film.

3. Iodized oil is of value in depicting the uterine and tubal lumina. Its chief value lies in locating the site of tubal ob-The information it yields concerning uterine pathology is often incomplete because the latter alters the organ contour more than its lumen.

Iodized oil instillation is practically useless in diagnosis of ovarian pathology.

Iodized oil and pneumoperitoneum combined vields the maximum information regarding the pelvic organs short of intraperitoneal exploration, and is indicated in a carefully selected group of cases.

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DISCUSSION

Dr. Wintz¹ (Erlangen, Germany): The roentgenologic method of diagnosis represents unquestionably a remarkable progress in gynecology, because there are cases in which diagnosis by palpation fails owing to special circumstances. There are also cases in which the simple bimanual examination does not lead to the desired result because the somatic changes are much too slight. As cases where the roentgenologic method of diagnosis seems specially indicated, I may (1) Patients with specially developed adipose tissue or women who could otherwise be examined only rectally; (2) Adnexal tumors, the contents of which are not tense, especially many tuberculous cases; tuberculiform swelling of the fimbriated end without formation of larger tumors; ad-

discussion, prepared by Dr. Wintz, was read by 1This discussion, Dr. R. H. Stevens

hesions in the small pelvis and the adjacent organs which are not palpable; (3) Differential diagnosis between fixed and mobile position and support of the uterus, between adnexal tumors and malformations, between myomas and malformations, myomas and adnexal tumors, separation of the adnexal tumors, tubal pregnancy and twisted pedicle; differentiation of teratoid ovarial tumors and par-ovarial cysts; differential diagnosis between myoma and pregnancy, between parametritis and adnexal tumor; diagnosis of defective formations and malformations; significance of the adhesion-diagnosis; also for the X-ray therapist.

Two methods are to be considered for gynecologic X-ray diagnosis: The pneumoperitoneum and injection of a contrast filling.

In our technic we use, instead of lipiodol or iodipin, contrastol, a preparation developed in my chemical laboratory by my assistants, Dr. May and Dr. Dyroff.

Contrastol is a bromide preparation in which the bromide and oil are so closely combined that heat, even up to 170 degrees Centigrade, will not decompose it. From lipiodol, which we used for our first X-ray plates, iodine is liberated even at a temperature of 95 degrees Centigrade. Although this is inconvenient for sterilization it would not render this preparation unsuitable to be used in the human body, but iodine is also liberated by physiologic acids and alkalies, for instance, the gastric juice.

If lipiodol is used to fill the tubes, there is a possibility of injuring them by the irritation of the liberated iodine, and should the preparation reach the peritoneum, the iodine is quickly absorbed. Both these harmful effects have been determined.

The harmlessness of our preparation, contrastol, however, has been proved. It is possible to show the excretion of bromide in the urine by means of Garnet's fluorescin test. The excretion takes place constantly in small quantities.

With regard to our method I want to emphasize that the filling must be done without undue pressure, because, if the injections are made under pressure, there is the danger that inflamed agglutinations in the tubes may be severed. Thus even an artificial peritoneal infection would be possible which must be absolutely avoided in a diagnostic method. Pressure in filling must further be avoided for the reason that a widening of the tube-bag may take place in case the tube itself should be closed. In such a case the real dimensions and forms would be obscured. I think the proper way to fill the tubes is by physiologic forces. namely, by the contractions of the uterus itself, while the mouth of the womb (os uteri) is open. It is important, therefore. not to overtax the capacity of the uterus. Consequently one injects only until the medicament starts to flow back from the mouth of the womb. It is further necessary to make the injections with such care that the irritation does not cause the uterus to contract.

The films taken with such precautionary measures have given us an important insight into the physiology of the genitals. They have enlightened us about the capacity of the uterus and especially about the movements of the tubes. With regard to differential diagnosis, the X-ray films showing the tubes filled are especially important for the representation of the closure of the tubes.

Dr. B. H. Orndoff (Chicago): I cannot discuss this paper critically but I desire to commend it in every way.

This work has a very great scientific value in medicine, coming from the well-directed clinics of Dr. Stein and Dr. Arens; one is impressed with the unusual accuracy in diagnosis that is offered their patients. This degree of accuracy cannot be reached by a consideration of history and physical findings, but requires technical intervention. Certainly no method has given so much information about the oviducts.

The technic I have employed in this work varies to some degree from that described by the essayist, in that we mainly employ fluoroscopic observations while the opaque material is maintained within the uterus and oviducts under pressure and while bimanual digital examination is being conducted. In this manner we determine mobility, fixation, and other findings which we believe to be of considerable clinical importance.

Again, let me express my appreciation for having heard this unusually valuable contribution.

Dr. Stein (closing): Just one word in addition, to urge that cases that have been examined with lipiodol should be studied

pathologically whenever possible. Naturally the gynecologist has the advantage over the internist of examining some of his material pathologically before autopsy. Fortunately for the internist, his chest cases are not necessarily sectioned soon after instillation of lipiodol. However, I think they should be followed whenever possible to the pathologist's laboratory. Only after several years' experience will we learn whether the iodized oils are entirely harmless to the human tissues. I hope we will find that they are. In answer to the question that Dr. Orndoff brought up as to method, the fluoroscopic versus the film method of study-our object is to avoid excessive fluoroscopy from the standpoint of protecting the operator, if we feel satisfied that we can learn as much from the film method. I again wish to thank the members, and particularly Dr. Wintz and Dr. Orndoff, for their very kind discussion.

By ARTHUR W. PROETZ, M.D., and EDWIN C. ERNST, M.D., SAINT LOUIS

SEVERAL months ago one of us (A. W. P.) described a new and simple procedure for the introduction of fluids into the nasal sinuses without puncturing or otherwise injuring their walls.

"Displacement irrigation" is the name applied to the method, as it was originally devised for the treatment of sinusitis with various solutions. Its adaptability to the injection of iodized oils soon became apparent, particularly for the study of the posterior sinuses, which are most difficult of access by the usual methods.

The maneuver is exceedingly simple. It consists, briefly, in placing the head in such positions that the sinus in question shall be in relation to the nethermost portion of the nasal chamber, with its ostium upturned. The iodized oil is then floated into the nose from a syringe, and, finding its lowest level, comes to rest on the face of the sinus wall, submerging the ostium. It fails to enter the sinus at this point because normally the ostium is of insufficient size to permit of the influx of oil and the escape of air at the same time. Gentle suction is now applied intermittently to one nostril, the other being closed with the finger. The palate and tongue are held in the "K" position to seal the pharynx.

On applying suction a bubble of air is withdrawn from the sinus through its upturned ostium. On releasing suction this displaced air is replaced by a drop or two of the overlying fluid. The process is repeated until the desired amount of oil has been introduced: about fifteen or twenty alternations are usually sufficient. The patient is returned to the erect position and the fluid remains in situ for an indefinite peri-

od, depending upon the characteristics of the individual nose (four hours to several days). The whole procedure occupies about a minute. PR

While the principle is exceedingly simple, certain details of technic should be observed. Our own present routine is set down here as a guide and without any pretense at finality.

POSITIONS FOR INJECTION

Two major positions are employed. The first and more important is the spheno-ethmoid position, so called because it places the cells named in the dependent relation to the nose and permits them to fill, primarily. The patient lies flat on his back with the head extending beyond the edge of the table and hanging down, so that the chin is directly above-that is, in a vertical plane with-the external auditory meatuses. In this position the most dependent portion of the nasal chamber is a pocket formed by the face of the sphenoid and the cribriform plate of the ethmoid (Fig. 1). The nasal chamber, thus placed, will ordinarily accommodate 5 mils. of oil without overflowing either through the nostrils or into the pharvnx (Fig. 2). If suction is now intermittently applied the 5 mils. of oil will properly fill the sphenoid and posterior ethmoid cells (Fig. 3), the combined capacity of these cells averaging about 12 mils., but varying widely in individuals (6, 10).

If now another 5 mils. of fluid is introduced and the suction repeated, the maxillary sinuses, the anterior ethmoids, and sometimes the frontals will be partly filled. For a general examination of the sinuses, injection in this one position may suffice. Fig. 8 shows the distribution of oil introduced in this way.

¹Presented before the Radiological Society of North America at the Twelfth Annual Meeting, at Milwaukee, Nov. 29-Dec. 4, 1926.

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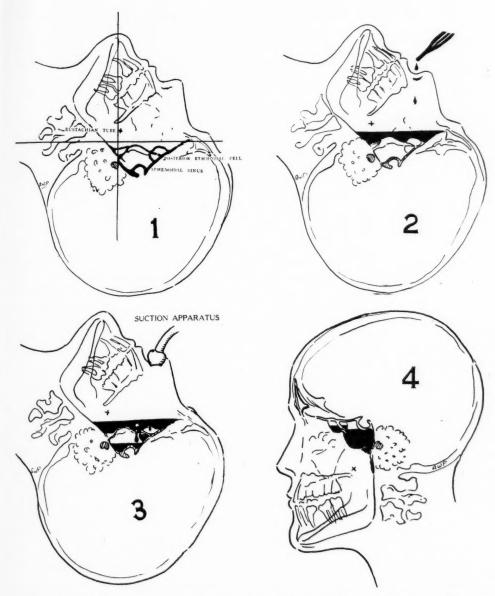


Fig. 1. Diagram indicating the correct position of the head for displacement irrigation. (The parts immediately concerned are heavily outlined.)

Fig. 2. Second step. The introduction of fluid into the nostril. It comes to rest in the nasal chamber but does not enter the sinuses.

Fig. 3. Third step. Intermittent suction is applied at the nostril. Air bubbles are withdrawn from the cells, and are replaced by drops of the overlying fluid. Sphenoid and posterior ethmoid cells are shown filling separately. shown filling separately.

Fig. 4. Patient returned to the upright position. The fluid remains in the sinuses.

In filling only the posterior cells none of the oil enters the pharynx so long as the proper position is maintained. On introducing the second 5 mils., however, some of it may enter the oropharynx and the patient



Fig. 5. The prone position for displacement of the anterior group of sinuses. The parts concerned are heavily outlined. If the nasal chamber is filled with oil to the level of the dashed line, all the ostia are submerged without spilling oil over the posterior margin of the septum.

should be instructed not to swallow it. It is helpful with a child or a difficult subject to instruct him to open his mouth wide, and breathe through it during the whole process. This shuts off the pharynx and renders swallowing impossible. A gag may be resorted to if necessary.

After injection the patient is returned to the erect position (Fig. 4) and requested to clear his throat of superfluous oil before the films are taken.

The second position is the prone position. It is employed for injecting the frontal, anterior ethmoid, and maxillary sinuses. The patient leans forward or lies face down on a table with the nasofrontal suture and the upper incisors in the same horizontal plane.

Two or three milliliters of iodized oil are now introduced into one nostril with a syringe which fits it closely. On withdrawing the syringe the nostril is held shut with the finger to prevent the escape of the oil. Intermittent suction is now applied to the other nostril until the oil has entered the sinuses. More oil is introduced if desired and the process repeated. Injection in this position is accomplished by virtue of the anatomical relation of the posterior margin of the septum to the ostia of the sinuses, as indicated in Fig. 5. With the head in the prone position it is possible, by filling one nasal chamber through the nostril, to submerge all the ostia before any of the fluid spills over the posterior margin of the sentum into the other chamber. This septal barrier, therefore, keeps the opposite nasal fossa free from oil and available for the application of suction.

The frontal sinus is the most difficult to fill as its outlet is long and narrow and bubbles of air are not readily displaced from it. This condition exists also, and fortunately to an exaggerated degree, in the middle ear and the eustachian tube. This tube is a collapsed membrano-cartilaginous passage in its pharyngeal portion, and so narrow that no air is withdrawn from the middle ear when the vacuum is applied. We have been unable to introduce any fluid into either the middle ear or the tube by this method, which is well, as it eliminates the likelihood of infecting them with organisms from the nose.

In both positions it is necessary to introduce the oil into the side to be studied. In the spheno-ethmoid position it happens that enough fluid finds its way into the opposite nasal fossa to fill some cells. But the patient may clamp down his pharynx so tightly that this does not occur, and if both sides are to be injected it is preferable to distribute the fluid equally between them. In the prone position the oil should be confined, of course, to the side of its introduction.

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Several of the halogenized oils have been introduced by this method; the various pastes and suspensions of insoluble radiopaque salts are obviously unsuited to it. Aside from the difficulty of introducing the

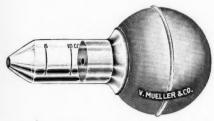


Fig. 6. Special syringe for introducing lipiodol and producing suction. The rubber bulb is of such thickness as to create only the necessary degree of vacuum.

latter it is doubtful whether the introduction of a semi-solid foreign body into a sinus is advisable.

The oil which proves most satisfactory in our hands is lipiodol, diluted with an This mixture equal volume of olive oil. combines optimum fluidity and density and -quite as important-is bland and unirritating to the mucosa. This is not true of some other iodized oils. Solutions employed in this work must be non-irritating and stable in their composition, for, be it remembered that, unlike mere nasal injections, these fluids may rest in contact with the delicate lining membranes for several Following the mildest irritation, headaches result, which continue as long as the fluid remains. These have not been encountered since the above mixture was It is unnecessary to warm it, adopted. though this assists somewhat in introducing it where much swelling is encountered.

The diluted lipiodol (iodine content 20 per cent) is preferable to the undiluted oil, as the reduced opacity sometimes reveals

filling defects which are lost in the denser shadow.

Lately we have flushed the nasal chambers with liquid petrolatum after the injection and before making the plates. This oil, itself transparent, removes traces of lipiodol which cling to the turbinates.

Five milliliters of the opaque oil to each side is usually sufficient. It seems to us that a partial filling of the sinus is preferable to a complete one, as the fluid levels resulting in the former case serve to distinguish overlapping cells.

SUCTION APPARATUS

Any vacuum appliance will serve to produce suction for this maneuver, provided that the vacuum can be controlled, not to exceed 180 mm, of mercury.

One of us (A. W. P.) has devised a simple rubber-bulb syringe (8) with a short, wide glass barrel calibrated at 5 and 10 milliliters. This syringe serves the double purpose of introducing the oil into the nose and producing the vacuum. Its rubber bulb is designed to maintain the proper tension.

ADVANTAGES OF THE METHOD

Beyond the obvious value of iodized oils in sinus work, this method of introducing them has certain advantages over the usual injections.

It is frequently impossible to locate the ostium of a sinus, especially in the presence of hyperplasia, and puncture must be resorted to. This in itself is undesirable, aside from the obvious fact that only those cells which are encountered by the trocar are injected. By the displacement method the oil itself seeks them out. All cells from which a bubble of air can be extruded are at least partly filled (9), and from this circumstance arises an important diagnostic indication; namely, that the facility with



Fig. 7. Shows patient in spheno-ethmoid position and indicates the extent to which posterior cells are filled with 5 mils. of oil.

which the oil-penetration occurs is a direct index of the patency of the ostia. Not only can general obstruction to drainage be demonstrated but individual cells are shown to be obstructed while others are clearly free. Many cases are encountered in which a posterior ethmoid sinus, for instance, fills readily, while its adjoining sphenoid fails to fill at all, although the oil levels in the normal cells show the head in the proper posi-

tion and the diseased ostium properly submerged.

It is possible, also, when only a single sinus is under investigation, to confine the oil employed largely to that sinus by applying astringents to its ostium without shrinking the rest. Varying the posture of the head with a view to singling out a desired sinus is not effective and may spill the oil into the pharynx, causing the patient to gag.

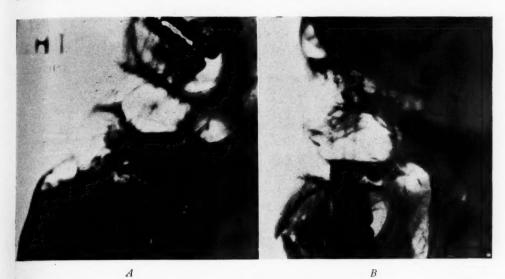


Fig. 8. Shows the extent to which the sinuses may be filled with 10 mils. of lipiodol introduced in the spheno-ethmoid position. (A) Shows the patient in the supine position; horizontal beam. (B) Erect position; horizontal beam.

Much incidental and unexpected information may be gleaned from this method which is of value to the rhinologist. We have succeeded, for instance, in outlining a rather extensive post-operative synechia in

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the region of the olfactory fissure—not only as to its extent, but as to its thickness as well. Sphenoids have been encountered whose pneumatized pterygoid processes extend significantly near the eustachian tubes,



Fig. 9. Films obtained by introducing 3 mils. of oil in the prone position, mapping the anterior ethmoid cells on the right side alone.

as Sluder lately pointed out. Others have been observed which filled with difficulty or not at all, but which after a course of treatment permitted normal penetration.

It is useful, further, in determining the

RADIOGRAPHIC CONSIDERATIONS

The diagnostic information obtained by this method is essentially dependent upon the correct position of the head in relation to the X-ray beam and film.

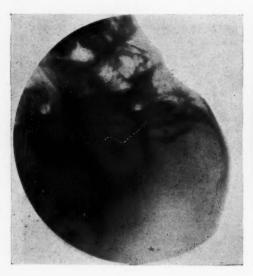


Fig. 10. Shows failure to penetrate sphenoid cells although ethmoids are filled. The film shows the position correct and the oil in ample quantity to fill sphenoid. Failure of the sphenoid to fill is due to obstruction of the ostium. This was overcome by treatment and complete filling obtained.

true relations of the two groups of ethmoid cells. The terms "anterior" and "posterior" as applied to the ethmoidal labyrinth are unfortunately chosen. According to the prevailing usage, "anterior ethmoid cells" are those which open into the middle meatus; "posterior ethmoid cells" open into the superior meatus. Now it frequently happens that a cell opening into the middle meatus, and therefore characterized as "anterior," extends around and behind one which opens into the superior meatus and is called "posterior," and vice versa. By filling only one group with opaque oil, its ramifications and their relation to the other group may be studied.



Fig. 11. Sphenoid half filled, spheno-ethmoid position, showing intrinsic filling defect of sinus. Note thin white line along the roof as well as translucent mass on floor of sphenoid.

It is not always possible nor desirable to completely fill the sinuses with the iodized oil, and consequently a partial or absolute rotation of the head is necessary to exclude filling defects or inflammatory changes of the wall.

The horizontal X-ray beam is the more valuable tube position for outlining the superior, inferior, and lateral sinus walls.

In examining the sphenoid and posterior ethmoid sinuses the initial lateral exposure may be made in the identical position of the introduction of the oil, namely, the sphenoethmoid position, the patient remaining supine, the head angulated backward so that the chin is in a superior vertical plane with the external auditory canals.

A second lateral film should then be made in the reverse position, the patient sitting erect with the chin down and still in a ver-

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tical plane with the auditory canals, the Xray beam, however, remaining in the same lateral horizontal direction.

Other positions of the head and tube may he employed in special cases: for example, the Granger, Pfahler, Hirtz, Waters, Pirie,

and Aspray angles.

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The study of the frontal and maxillary sinuses will require slight variations in radiographic technic. The posterior anterior view in studying the maxillary antra will be found to be an additional valuable diagnostic position.

For the average lateral skull examination we have adopted a comparatively simple radiographic technic, limiting the fine focus radiator tube to 10 milliamperes and five seconds exposure. The average potential approximated 76 to 80 K.V. (4½ inch spark gap), at an anode film distance of 28 inches. The exposure time was doubled in the posterior anterior or semilateral views. By means of this radiographic formula clear and distinct radiograms are uniformly The diagnostic value is relaobtained. tively dependent upon sharp and contrasty negatives, showing absolutely no movement. Therefore, complete immobilization is the final radiographic requisite in the various positions of the head above described.

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DISCUSSION

DR. C. G. SUTHERLAND (Rochester, Minn.): We have had a very limited amount of material for two reasons: first, the neurological and neurosurgical sections feel that the localization of cord tumors has been satisfactory with present methods; and, second, there is still a question as to risk in injecting material into the spine which is not absorbed. This objection is supported in a recent article by Maclaire, in which he states that in one patient on whom he operated he found encysted lipiodol which had been producing symptoms. In his opinion, lipiodol should be injected for localization only in cases in which laminectomy is to be done almost immediately, thus allowing exit of the lipiodol from the spinal canal.

DR. AMEDEE GRANGER (New Orleans): It was my privilege to listen to Dr. Proetz' paper in Dallas during the American Medical Association meeting, and I was very much impressed with the possibilities offered for confirming the diagnosis made by the method which I have been advocating. I experienced some difficulty in obtaining the lipiodol for a time, and in getting the otolaryngologists in New Orleans to try his

method. They seemed to be quite satisfied with the diagnoses we were giving them and were rather reluctant to use the lipiodol at all. My experience is limited to a very small number of cases in which pathology of the sphenoid had been diagnosed by our method. The lipiodol got into the posterior ethmoid but it did not get into the sphenoid in any of the seven or eight cases in which it was used. Rather discouraged by that, I induced two otolaryngologists to attempt the injection of the lipiodol into the sphenoid with a Sluder needle. In the first case, which we had diagnosed chronic hyperplastic sphenoiditis, the lipiodol was injected into a large posterior ethmoid as was clearly demonstrated by the study of the views made in the lateral and in our positions. The otolaryngologist thought that he was in the sphenoid, because the needle went through a definite bony partition, and, after that, its end was freely movable. In the case of the second patient he was more fortunate: the lipiodol got into the sphenoid and could be seen, kept away from the Granger line by the thickened membrane, which had been said to exist after a study of the negatives made according to our technic. We had prophesied that this would happen in cases of hyperplasia, and Dr. Proetz has showed us some slides in which the same thing occurred with different portions of the sphenoid wall. It was most interesting to note that in both of these patients the therapeutic result was more than had been hoped for even. The last patient had the typical sphenoid syndrome, and a headache from which he had been suffering for two or three years. The attacks had been increasing in frequency and in severity for about a month before the treatments, and the headache was almost constant for the past week or ten days. He was seen three weeks after the injection and stated that he had been absolutely free of headache since forty-eight hours following the injection.

Dr. ALTON OCHSNER (Madison, Wis.): I agree heartily with Dr. Pritchard² in that the method we use in introducing lipiodol into the bronchial tree should be as simple as possible. I agree that observation should be done with a fluoroscope. At the University of Wisconsin we have been using a method which we consider extremely simple, no special instrumentation being required. The method depends upon a simple knowledge of physiology. We anesthetize the patient and break the reflex act of swallowing, so that the oil when taken into the larynx cannot pass down into the esophagus, as it normally would do, but passes into the trachea. The only instruments used are one or two swabs, two sterile medicine glasses, a cocaine solution, and lipiodol. We have done this in over two hundred cases and have never had a patient object to a refill. It is extremely simple for the physician. It is not necessary to use a hand mirror or light of any kind; we merely anesthetize the palatine arch above the base of the tongue, being careful not to let the anesthetic flow down and anesthetize the esophageal orifice. By keeping the anesthesia high, we break the reflex act of swallowing, and the lipiodol, when taken into the larvnx, passes down into the trachea. We feel that the mode of filling, watching the oil fill the bronchus, is more important than the interpretation of the plate. We feel that it is one of the decided advantages of the technic to introduce the oil while the patient is under the screen. We feel that the iodized oil has a distinct therapeutic value. have been able to show that a large series of cases, cases with bronchial dilatation, have been completely cured following repeated

²This paper by Stuart Pritchard, Bruce Whyte, and J. K. M. Gordon will be found in RADIOLOGY, February, 1927.

injections of iodized oil. This method can he repeated as many times as necessary, and, as I said, we have never had an individual object to a re-fill, which is more than can be said of some of the other procedures. The technic is extremely simple. larvnx is anesthetized, and as soon as it becomes immobile, we have the patient placed before the screen and he is given the lipiodol and instructed to shift the head back and lean to the side we wish to fill. The patient is instructed to breathe, the lipiodol is aspirated, and it can be seen entering the trachea and the bronchial tree on the desired side. If we desire to fill the upper lobe, the technic is the same. As soon as the lipiodol enters the trachea, the patient is tipped over to one side so that the chest is kept lower than the trunk, allowing the lipiodol to be aspirated and to run by gravity into the upper lobe.

DR. PROETZ (closing): I wish to thank Dr. Granger for the pains he has taken in trying out my method. One thing I forgot to mention: we find that in those pathologic conditions where the ostium is closed, if we shrink the nose with cocaine or some other astringent, we are often able to get the fluid into sinuses which it would not otherwise enter.

THE USE OF DENTAL FILMS IN THE DETERMINATION OF STRAY RADIATION¹

By R. S. LANDAUER, Ph.D., CHICAGO

THE need of ascertaining, at least with some degree of accuracy, the quantity of radiation which a roentgenologist is receiving during the operation of his X-ray machine is quite evident. During

any opinion as to how much radiation he is receiving in terms of erythema dosage.

The purpose of this paper is to give a simple quantitative answer to this problem, by exhibiting to you some films which have

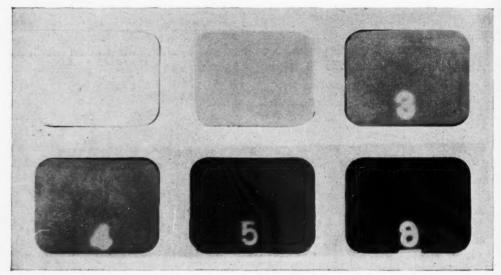


Fig. 1. See page 513.

several years past, the author has come in contact with many roentgenologists and in the course of even a short conversation, the question of protection against stray radiation is almost invariably discussed. All agree that sufficient protection must be employed but few seem to know whether or not they have enough. Almost everyone, at one time or another, has carried dental films on his person for varying lengths of time, and then developed them. A more or less darkened film usually results. But what does this darkening mean? The roentgenologist is usually at a loss to form

been exposed to known fractional parts of the erythema dose. Since this paper was originally written, there has appeared in RADIOLOGY (September, 1926) an admirable paper by Edith Quimby on the same subject. I feel, however, that too much emphasis can not be placed on this important subject. That reason, as well as the fact that I have the actual standard films on exhibit, seems sufficient justification for presenting this much more brief work.

The necessity for protection can not be over-estimated, and yet, too much in lead or lead equivalent is bulky and costly. With the great variation in X-ray output from

¹Read before the Radiological Society of North America, at Milwaukee, Nov. 29-Dec. 4, 1926.

one installation to another, it seems inadequate to attempt to apply any formula for calculating the amount of radiation the operator is receiving. This radiation must be measured directly and integrated over a period of time and position. A means for so doing is best offered by the use of dental films. The problem then resolves itself into two parts: first, the tolerance of the roentgenologist to stray rays, and, second, the determination of what fraction of an erythema dose is represented by a definite blackening on the film.

It is not the primary purpose of this paper to state the amount of X-ray which may be received and tolerated, but rather to give the roentgenologist a measure whereby he may know how much he is receiving in terms of erythema, that he may, from his own clinical knowledge, decide whether or not it is too much. However, in order to have some starting point, the author has decided to adopt, as an approximation, Dr. Mutscheller's value. The latter has stated that 1 per cent of an erythema dose per month would be a safe tolerance dose. We

may consider, then, that all films representing more than 1 per cent of an erythema per month, represent conditions of inadequate protection.

I have made a series of standard films representing fractions of erythema doses from 0.02 per cent to 1.2 per cent. Each step in this series is readily distinguishable from all others by simple visualization.

I do not feel that such accuracy as is obtained by the photo-electric cell method of Ouimby is necessary in the average laboratory. Small variations in the film density have no practical value, when, as in the present case, it is a question of order of magnitude rather than small percentages in which we are interested. Since the main purpose of this investigation is the determination of stray radiation in laboratories where therapy is being administered, the quantity of X-ray reaching the film is described both in erythema dose and in e-units. The e-unit taken is that described by Beets and Arens as that quantity of X-ray which, by the ionization produced in 1 c.c. of air traversed by the X-ray, per-

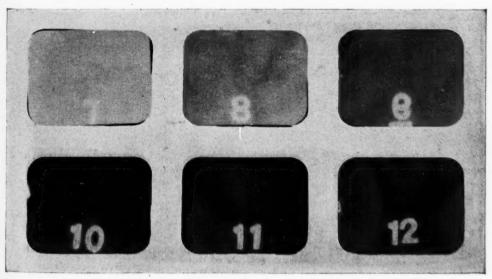


Fig. 2. See above.

mits 1 E.S. unit of electricity to be transported across an electric field under saturation conditions. Three different degrees of hardness of rays were used-those produced by 125 P.K.V. and 6 mm. Al., having a half value of about 8; those at 150 P.K.V., 1/4 mm. Cu., with a half value of about 10, and those at 200 P.K.V., 1/2 mm. Cu., with a half value of about 12. The number of e-units necessary for an ervthema dose in the first case is 1,000, in the second 1.200, and in the last 1.600. The darkest film obtained. No. 6, received 2.8 e-units, or 0.28 per cent of an erythema dose-less than one-third of the previously described tolerance dose. Thus, if a roentgenologist carried a film on his person. when being exposed to stray radiation filtered by at least 1/4 mm. Cu., for ten days, and found it as black as No. 6, he would then know he was getting a little less than a tolerance dose, or, in other words, would be operating under conditions of safe protection.

A second group of films was exposed to unfiltered radiation. In this case, the films are described in terms of percentage of a McKee erythema, as this unit is the most widely used in determining unfiltered radiation.

In this case it will be noted that the films representing equal fractions of erythema doses with the filtered dose are much lighter, showing that less unfiltered than filtered ray may be tolerated.

EXPERIMENTAL

An X-ray machine and Coolidge tube were operated at a known voltage and milliamperage, and an accurately measured filter placed in the beam of X-rays. The quantity of rays reaching a given distance was measured by a direct reading roentgenometer, previously standardized in e-units. Films were then placed in the position occupied by the front surface of the ionization chamber and exposed for varying lengths of time. By this procedure, the films were exposed to known fractional parts of erythema doses. The films used were Eastman Regular Dental Films and

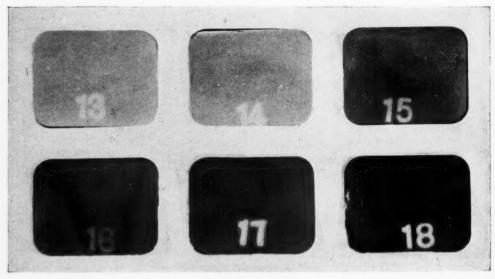


Fig. 3. See page 513.

were developed all together and at the same time in fresh full strength Eastman X-ray Developer for five minutes at 65 degrees Fahrenheit.

The accompanying table and film reproductions (Figs. 1, 2, and 3) give the results of this work. For example: the machine was operated at 125 P.K.V. (8½ inches), 5 millimeters aluminum filter, 5 milliamperes, and 15 inch distance. Under these conditions the machine was found to be delivering 810 *e*-units per hour. An erythema dose with these factors is 1,000 *e*-units.

Film No. 4 was exposed for six seconds. 6 x 810

In this time it received $\frac{1}{3,600}$, or

1.3~e-units. Since 1,000~e-units are required for an erythema, the film received

an equivalent of $\frac{1.3}{1.000}$, or 0.13 per cent of

an erythema dose. Thus, if a film carried for a week became as black as No. 4, it would indicate that the carrier was receiving radiation at the rate of 0.13 per cent per week, or approximately 0.5 per cent per month—only one-half of the tolerance amount.

A quantitative determination in accordance with the above scheme may be made in

any laboratory. The author will be pleased to send to any one interested, a film made from the standard representing 0.28 per cent of an ervthema dose. The roentgenologist will then place one or more Eastman Regular Dental Films at strategic points, that is, in the control booth and in his pockets, and operate his machine in its routine fashion. The films should be left in place for nine days and then developed in fresh developer at exactly 65 degrees Fahrenheit and for exactly five minutes. One of two cases arises. If the film is darker than the standard, representing 0.28 per cent of an ervthema, it means that the roentgenologist is receiving more than 0.28 per cent of an erythema in nine days and more than 1 per cent a month. Here lack of sufficient protection is indicated.

The second case is one in which the film is less dark than the standard—this, then, would mean safety. While there will be some error due to the fact that the standard and test films are not developed at the same time, yet if the above technic of development is accurately carried out, this error should be so small as to be negligible.

A study of the accompanying table shows that minute fractions of an erythema dose register on dental films as a considerable darkening and unless the equivalent ery-

TABLE SHOWING FRACTIONS OF ERYTHEMA DOSES REPRESENTED ON ACCOMPANYING FILMS

No. P.K.V. Ma. Dist. Filter e-units per hr. e-units for Time of e-units. Per-

No.	P.K.V.	Ma.	Dist.	Filter	e-units per hr.		Time of		Per-
of			(in.)		delivered by	dose	exposure	on film	centage
film					machine		of films		ery. on
							in seconds		film
1	125	5	15	6 Al.	810	1,000	1	0.225	0.022
2	125	5	15	6 Al.		1,000	2	0.45	0.045
3	125	5	15	6 Al.		1,000	4	0.90	0.090
4	125	5	15	6 Al.		1,000	6	1.35	0.13
5	125	5	15	6 Al.		1,000	10	2.25	0.22
6	125	5	15	6 Al.		1,000	12	2.80	0.28
7	150	5	15	0.25 Cu. and 1 Al.	1,000	1,200	2	0.55	0.046
8	150	5	15	0.25 Cu. and 1 Al.	,	1,200	4	1.10	0.092
9	150	5	15	0.25 Cu. and 1 Al.		1,200	6	1.65	0.138
10	150	5	15	0.25 Cu. and 1 Al.		1,200	8	2.20	0.184
11	150	5	15	0.25 Cu. and 1 Al.		1,200	10	2.75	0.224
12	150	5	15	0.25 Cu. and 1 Al.		1,200	12	3.30	0.276
13	200	5	20	0.52 Cu. and 1 Al.	1,030	1,600	4	1.15	0.072
14	200	5	20	0.52 Cu. and 1 Al.	1,000	1,600	6	1.72	0.108
15	200	5	20	0.52 Cu. and 1 Al.		1,600	8	2.30	0.144
16	200	5	20	0.52 Cu. and 1 Al.		1,600	10	2.86	0.180
17	200	5	20	0.52 Cu. and 1 Al.		1,600	12	3.44	0.216
18	200	5	20	0.52 Cu. and 1 Al.		1,600	18	5.15	0.32

thema is known, much needless alarm may be caused.

DISCUSSION

DR. OTTO GLASSER (New York): Dr. Landauer's paper touches upon an extremely important problem, that of proper protection for the radiologist. Adequate protection is absolutely essential and every step towards reaching this goal is welcome. The method, as Dr. Landauer has mentioned, is not new. Dr. Pfahler, Mrs. Ouimby and others have employed a similar way to measure undesired radiation. Yet it seems that Dr. Landauer's modification of the method is a step forward, because it is extremely simple and for that reason may come into more general use. But just on account of this simplicity, we have to discuss whether or not the method is accurate enough. From a strictly scientific point of view, where we are dealing with an accuracy of better than 1 per cent, this method, of course, could not be satisfactory. individual comparison of the darkening on an exposed film with that on a standard film is relatively inaccurate. The fact that the film exposed to the undesired radiation collects rays of a most heterogeneous character, while the standard exposure may have been made with an entirely different radiation beam, is one of the factors that probably will not permit an accuracy of better than 50 per cent. But for the purpose for which the method is suggested, this accuracy for the time being is entirely sufficient. For more exact requirements, such as, for instance, measurement of the direct roentgenray dose, it would not be sufficient (Kienboeckstrip!). As far as the collection of protection data is concerned, the method may help us to arrive at a closer approximation of the so-called tolerance dose. Dr. Mutscheller recently proposed a value of one-tenth of an erythema dose per year as a

tolerance dose. It would seem valuable to corroborate this value by carrying out a large number of observations in many Xray laboratories, perhaps by means of Dr. Landauer's method, that we might come as close to an approximation of the tolerance dose as possible. In this connection one point may be important: that is, the fact that a film probably will accumulate a certain dose of inhomogeneous rays in a different way than the human body does, so that it may seem hard to correlate a certain darkening on a film with the effect on the entire body. Still, I think Dr. Landauer's method should come into general use, since very likely it is accurate enough, and if generally used would lead to more satisfactory data on the protection question than we have at our disposal to-day.

DR. G. E. PFAHLER (Philadelphia): You all know that I called attention to this little method of carrying dental films about five years ago in connection with my blood studies of radiologists, but the important thing is that you should aim to carry a dental film in your pocket for a week or two weeks without getting any blackening at all. If you do that, the degree of blackening will not concern you. If, within two weeks, you get definite blackening, without regard to the special degree, you are in danger and you had better protect yourself. Now that is the practical principle that I learned from many dental films that were sent in from the radiologists. I think we sent blanks to about twelve hundred, and I think we got three hundred back, or three hundred and fifty, but even from those I learned, when we compared the blood of these radiologists with the degree of blackening on their films, that very generally the man's blood condition corresponded to the amount of blackening. In other words, when you are getting definite blackening, increase your protection.

DR. M. J. HUBENY (Chicago): I am one of those timid roentgenologists. seems as though we have a conflict of interests between the man who uses and the man who designs the X-ray machine. Just recently I repeated an experiment I have done several times in the past few years. merely with the idea of re-affirming my past experience. I took a dental film and put it on top of the fluoroscopic table, put the natient on top of the table, put two dental films on top of the patient, put two underneath the fluoroscopic screen and two on ton, one on my apron and one on the upright vertical control—the aperture control -where, in this particular instance, with the aperture open, the film was a foot and a half away from the central beam of the X-ray. I exposed the films one second. They were developed, and, naturally, the only one that showed any evidences was the one directly on top of the table, which was black, as we would have a right to assume. I immediately repeated that experiment with a one-minute exposure, developed the films, and obtained the same results. only film that was black was the one on the aluminum directly on the table; in other words, in the direct path of the rays. I then performed another experiment with intensifying screens, putting one on top of the patient, one alongside of the aperture control, possibly a foot and a half away from the central beam. I made an exposure of one second, developed the films, and I think the one on top of the patient was just slightly blackened-I am not so sure about it. Then I exposed the same screens with new films for one minute, and got a spine on the one on top of the patient: the one on one side, a foot and a half away, did not show a thing.

Now, what I really want to bring out is this comparative value of radiosensitivity between a dental film and a fluorescent screen. I think Dr. Landauer's paper is very commendable, because it brings the fact before us that we all think it is a hazardous occupation and I really cannot disabuse my mind of that. I am personally quite convinced. I may be a monomaniac on that. However, the results of this experiment showed me that as soon as I put the fluorescent screen on one side, when I used the fluoroscope, I would immediately visualize the bones in my hand, not with one minute's exposure but immediately The things we have to consider are the variability of the human erythema, the susceptibility of the individual to the action of the X-ray, and that we are dealing with a part and not with the entire skin; not only that, but we are actually dealing with a third dimension.

DR. LANDAUER (closing): In regard to Dr. Glasser's remarks, I realize as well as any one that the method is one of approximation, but, as he says, if it is correct within 50 per cent, it is sufficiently accurate to tell whether or not too much ray is being received. Dr. Pfahler said that we should get no blackening at all. It seems to me that that would be a rather rare case. A roentgenologist, in working around an operating machine, especially when he is doing fluoroscopic work, is exposed to a certain amount of radiation, even though it may be simply back-scattering from the walls of the room, and if the films which he carries do show some blackening-which certainly most of them will show-he should know, in terms of ervthema value, how much that represents. I fully agree with him that if an operator can carry films on his person for two weeks and get no darkening, that will be an ideal condition, but I am sure that is a condition which is not met with in the large majority of cases. When darkening does occur, it is important that a roentgenologist should have some idea of what he is receiving.

MENSURATION AND LOCALIZATION BY MEANS OF THE ROENTGEN RAY'

By CLAYTON R. JOHNSON, M.D., Los Angeles, California

IN February, 1926, I presented a method of mensuration and localization, which seemed to be a definite step forward toward practicability.² As a result of this

quirements and actually bring to every radiologist a practical, useful method for mensuration and localization by means of the roentgen ray. of

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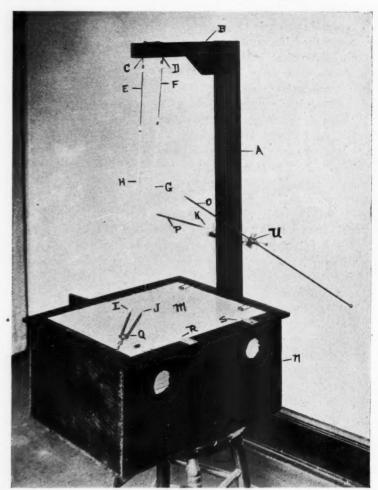


Fig. 1. See text.

work, another less complicated method has been devised, which, I feel, will meet all reThe special apparatus may easily be constructed in the average carpenter shop. Its principle is to reproduce mechanically, conditions which are identical with those in making stereoscopic radiographs. It consists of the following parts:

1Read before the Radiological Section of the Los Angeles County Medical Society, December 15, 1926.

2Johnson, Clayton R.: The "Radiogrameter." A Scale for Mensuration by Means of the Roentgen Ray, RADI-OLOGY, February, 1926, p. 136. Figure 1. "N" is a view box in the top of which is set "M," a ground glass, with dimensions 14 × 17 inches. "A" is a rigid vertical support to which is fastened "B," a horizontal support. The lower border of "B"

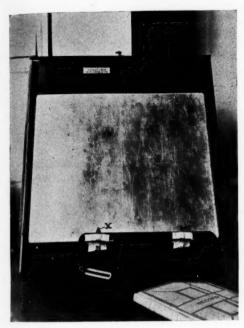


Fig. 2. See text.

is parallel to "M" and at a distance of exactly 25 inches from "M." "C" and "D" are very small holes, exactly 21/2 inches apart, drilled through "B" in such a way that a point midway between "C" and "D" will lie in a vertical line above the center of the ground glass "M." This center point on "M" must be accurately determined by dropping a plumb bob from a point midway between "C" and "D," with "M" perfectly level, and marked as the "radiographic center" of "M." "E" and "F" are 1/8 inch elastic bands arising from points "C" and "D," and fastened to "H" and "G," silk threads of contrasting colors. "Q" is an ordinary Eagle compass, the legs of which have been removed, and for which wooden pegs have been substituted. Ordinary steel sewing needles, "I" and "I," are driven into the wooden pegs. The silk threads "H" and "G" are then passed through the eyes of the needles and made of such a length as to be always under considerable tension regardless of what the position of the needles may be with relation to "M." "K" and "U" are universal joints supporting telescoping rods "O" and "P," the requirement being that the points of "O" and "P" may be easily placed in any position above "M" and will remain fixed. The universal joints were taken from a tube stand. The telescoping rods were devised from brass curtain rods. "R" and "S" are aluminum markers attached to "N" projecting over the edge of "M." These markers are the same in size and shape as the lead markers "X" and "Y" (Fig. 2), on the casette guide of the tray of the Bucky diaphragm, and are placed in the same relation to the radiographic center of "M" as "X" and "Y" are to the radiographic center of the Bucky diaphragm. This center of the Bucky diaphragm may be determined by dropping a plumb bob directly beneath the target of the tube when the target is midway between the two extremes of the stereoscopic shift.

In making the radiographs it is necessary that the tube stand be attached to the radiographic table. The Bucky table is ideal. In any event the target of the tube must always bear the same relationship to the radiographic center of the Bucky diaphragm for each setting, that is, in a vertical line above it. With the target thus centered at a distance of 25 inches from the film, make stereoscopic radiographs, using a longitudinal shift of exactly $2\frac{1}{2}$ inches. It is well to lay a metal bar of known length on the subject to be radiographed in order that a check can be made on the accuracy of the calculations.

From the above it will readily be seen that once a setting has been established for a given piece of apparatus, it may always be

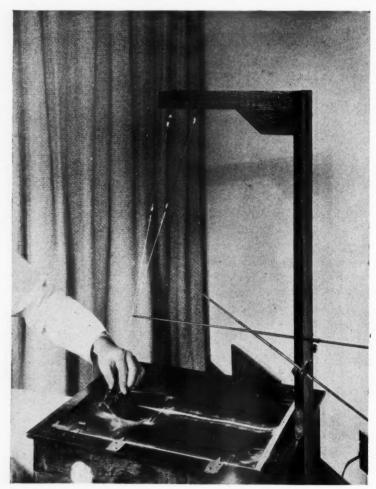


Fig. 3. See text.

duplicated with speed and accuracy. The plumb bob which has been used in previous methods is entirely dispensed with, and the only unusual marks to show on the radiographs are the shadows of the lead markers "X" and "Y."

In making the calculations from the stereoscopic radiographs, proceed as follows:

(1) Take one of the films and mark with ink dots the points on the shadows of the objects from which measurements are to be made, then superimpose the shadows of the second film on corresponding shadows of the first film, and mark corresponding points. The films will need to be shifted as each point is marked.

(2) Superimpose the films so that the shadows of "X" and "Y," respectively, overlay one another.

(3) Lay the radiographs thus superimposed on the view box so that the shadows of "X" and "Y" fall directly beneath the markers "R" and "S" (Fig. 3).

(4) Take the compass in the left hand, cross the silk threads once, and lay the eyes

of the needles over the ink dots representing the shadows of the point in question. The distance between the needles represents the shift in the shadow of the point. The point, as marked by the crossing of the threads, will then be the actual location in space, with relation to the radiographs, of the point in question at the time the radiographs were taken. Mark this location with the end of pointer "P." In like manner localize any other point whose location, with relation to point "P," is wanted, and mark its position with pointer "O." The desired dis-

tance or localization will then be as the relative positions of "O" and "P." This can be measured directly.

CONCLUSIONS

The method provides a rapid and accurate means of mensuration by means of the roentgen ray. As applied to pelvimetry, all the desired diameters of the pelvis may be determined in approximately ten minutes. Foreign bodies may be localized with relation to surrounding anatomical landmarks with like ease.

Light therapy of skin diseases in diabetes. -It is generally assumed that skin eruptions in diabetes are due to an irritation of the nerve ends by abnormal blood and serum compounds. Some investigations have also shown that exposure to ultra-violet light reduces the blood sugar. Any therapeutic effect in treating skin conditions in diabetes may be due. therefore, to this systemic indirect effect or to a local direct effect. The author relates the history of three cases of diabetes combined with pruritus, xanthoma, and mycosis, which show that the explanation is not so simple but, rather, that a direct and indirect effect are involved. The blood sugar of the pruritus patient was reduced by proper diet and insulin to 0.14 per cent (Bang); the itching continued. When the blood sugar reached 0.2

per cent, a few exposures to ultra-violet light stopped the itching completely. If half the body was covered during the light treatment, the other half responded promptly; the covered half, however, showed moderate relief. This points to a systemic indirect effect in addition to the local direct effect of ultra-violet rays. Similar observations were made in the other two cases. It is recommended, therefore, to try ultra-violet therapy in cases of non-diabetic xanthoma. Particularly striking seems the reduction of the cholesterin content of the blood in a patient suffering from xanthoma.

E. A. POHLE, M.D.

Light Therapy of Diabetic Skin Eruptions. St. Rothman. Strahlentherapie, 1927, XXIV, 465

EDITORIAL

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INTERNATIONAL GOOD WILL AND AMITY

Science requires that thought and action square up with facts as we understand them. Nothing is really definite, because the ultimate in time, space, and matter has not been reached. However, minds delving into the intangible, minds that are grounded on solid thought are apt to be stable—are not easily disturbed or disrupted by the emotional expressions of human nature, and, should they be so disturbed, the interval of adjustment is minimal.

Creeds and nationalities are abolished by purely scientific minds, therefore the most stabilizing influence in the world to-day is science.

RADIOLOGY has been enriched by contributions from men of scientific eminence all over the world, such men as Borak, Schüller, Forestier, Barclay, Reyn and others. They have favored us with their knowledge and some of them by their presence. We have learned to know them personally as well as by their accomplishments; thus are welded the links of tolerance, mutual understanding, and friendship.

It is hoped that this journal and this Society will continue to be media of expression of radiological knowledge. Thus are bred international good will and amity.

A COMMUNICATION

The undersigned has been commissioned to arrange a part of the program for the meeting of the Radiological Society next December. The subject assigned him has been the "Radiological Diagnosis of the Biliary Apparatus." Will all members who wish to participate in this part of the program kindly make application at an early date, indicating briefly what phase of biliary disease they wish to cover (hepatic abscess or other hepatic pathology, pancreatic disease, gall-bladder disease, cholecystography, etc.)?

James T. Case, M.D.

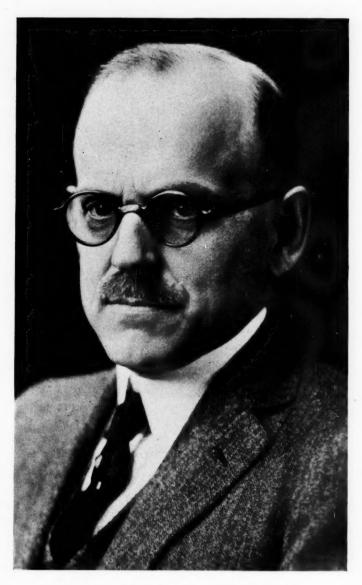
Battle Creek Sanitarium,

Battle Creek, Michigan.

HOMER CLIFTON MOSES

Dr. Homer Clifton Moses was born near Eaton, Ohio, on June 21, 1875, and died of pneumonia at his home in Colorado Springs, Colorado, on March 3, 1927.

He received his medical education in Bellevue Hospital Medical College, New York City, from which he was graduated in 1897. In 1898 he joined the United States Army as a surgeon and saw service in Cuba in the Spanish-American War. Later he was assigned to the Philippine Islands. In 1905 he became a resident of Colorado Springs, since which time he had been in active practice until May, 1925, when failing health forced him to retire. When the United States entered the World War he was one of the first to report at Fort Riley. Arduous physical training there broke down his health and his condition steadily declined.



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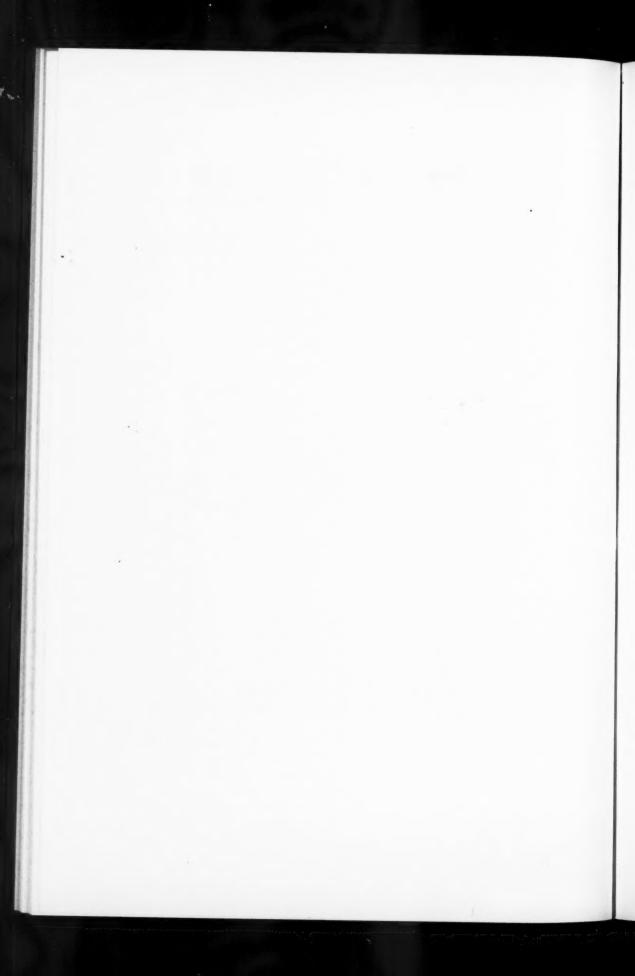
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EDWARD W. ROWE, M.D., LINCOLN, NEBRASKA President of the Radiological Society of North America



Dr. Moses was a member of the Masonic Lodge of Colorado Springs. While the Radiological Society of North America was still in its infancy Dr. Moses became a member and was active in the Society until about a year ago, when he was made an honorary member.

Doctor Wetterer, the Editor of *Internationale Radiotherapie*, has asked for the publication of the following announcement:

"It is intended to publish in the second volume of *Internationale Radiotherapie*, all courses given in roentgenology in any part of the world. This should enable everyone interested in post-graduate work to arrange his plans and get further information if desired. All in charge of such courses are requested to get in touch with Dr. J. Wetterer, Mannheim, 0.2, 1, Germany, regarding the insertion of their programs."

BOOK REVIEWS

OUR DOCTORS. A Novel of To-day. By MAURICE DUPLAY. Translation and Preface by JOSEPH COLLINS. Harper & Brothers, Publishers, New York and London, 1926. Price \$2.00.

A PSYCHOLOGICAL STUDY OF CANCER. By ELIDA EVANS, Author of "The Problem of the Nervous Child." With Introduction by Dr. C. G. Jung. Dodd, Mead and Company, New York, 1926. Price \$2.50.

THE PHILOSOPHY OF RADIO-ACTIVITY OR SELECTIVE INVOLUTION. BY EUGENE COLEMAN SAVIDGE, M.D., Member of New York Academy of Medicine, etc. William R. Jenkins Company, Publishers, New York, 1914. Price \$3.00.

While completing a sentence to physiologic rest (diabolical, I calls it), three new books have grouped themselves for comment.

"Our Doctors" is a new novel translated from the French by Dr. Joseph C. Collins, who seems to be taking several literary looks at the transparencies of literature, life, loves, and doctors. This is a darned good French novel but to physicians there is an unusual appeal and to those who take any interest in cancer there should be an intense interest. One satisfying quality is the correctness of all its medical, especially malignant, ideas and ideals. The dramatic situation of the doctor-hero, Daruel, finding a suspicious mass in the breast of his mistress while caressing her, is splendid. Daruel is a cold, superior, surgical genius whose ambition is to conquer that dread monster, Cancer. All the types of doctors are presented, from the charlatan and abortionist to the grand master with God-like qualities.

Now, where does this "Pyschology of Cancer" (Evans) enter this triadical arena of a one-eyed reviewer? Are there not enough unknown and hopeless slants to malignancy without injecting this latest flapper-craze of modern medicine, pyschology? But Elida Evans, disciple of Jung's Zurick school, hopes to offer fundamental pyschological origins for the later display in malignant cell rioting. Her case histories are records of unhappiness, grief, sorrow, and disappointments which were ultimately rewarded with the fatal kiss of malignancy.

The fundamental definitions and facts of psychology fill 200 pages of the book and lead the unfamiliar reader into mazes of misunderstanding or comprehension. Words -words-words! One is reminded of the volumes of hypotheses upon the nature and character of X-rays in the pre-Millikan days. But now that psychology has entered the etiological background of cancer we may expect the development of successively simpler explanations. ("Our Doctors"), the French author, engages his very practical doctor-hero with some of these thoughts when he wonders if his careless, often heartless, treatment of his mistress-wife could have been responsible for the appearance of the dread monster to shadow his successful, selfish career and eventually take his one great love from him.

The third book is one that is rescued from the ten-year-dead, scientific past with an apology. The title, "The Philosophy of Radio-activity" (Savidge), is the reason. The apology is that I never did and never will have sufficient knowledge, intelligence or what-have-you—or I—to appreciate this book. At first I actually thought it was a burlesque upon the intricacies of modern science, especially when I read the following passage: "Is the love of a ton of lead for the earth's center stronger than the nostalgia of matter for the rest period of its longest duration?"

But the flights of logarithmic logic will not surpass the flights of fancy of the novelist nor the imaginative analysis of the psychologist. Thus endeth the record of the tiniest slice of the thoughts that these volumes have aroused. You will read the novel ("Our Doctors") in one sitting (probably to 3 A. M.). You will read and reread the first chapter of the psychologic book and then jump to the case histories and begin to see the light of understanding breaking. And you will never be able to understand the "Philosophy of Radio-activity" unless a Rutherford or Millikan translates it into one-syllable words or de-bunks it entirely. Oh! why am I so ignorant? Ask me an--E. H. S. other!

ABSTRACTS OF CURRENT LITERATURE

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Roentgen rays and offspring.—Flaskamp sets forth the standpoint of the Wintz Clinic regarding temporary sterilization and injury to the offspring (see Strahlentherapie, 1926, XX, 79, 80). He emphasizes again that its performance is indicated in that type of cases of pelvic inflammatory diseases wherein menstruation aggravates the condition. It should be done only by well trained therapists, and in modernly equipped institutions.

Dyroff, from the same clinic, has undertaken a series of experiments on rabbits and guinea pigs, with carefully measured doses. He found the temporary sterilization dose for rabbits to be between 80 and 100 per cent E.D. (350 R), and for guinea pigs between 120 and 140 per cent E.D. (500 R). He comes to the conclusion that treatment of one parent only never leads to an injury of the offspring (observed to F_s). It was immaterial when the fertilization of the ovum took place in relation to the time of treatment.

E. A. Pohle, M.D.

Regarding the Question of Injury to the Offspring by Roentgen Rays. W. Flaskamp. Strahlentherapie, 1926, XXIV, 282.

Experimental Contributions to the Question of Injury to the Offspring by Roentgen Rays. R. Dyroff. Strahlentherapie, 1926, XXIV, 288.

Pathogenesis of cholecystitis.-Cholecystitis cannot be produced by placing organisms in the lumen of the gall bladder unless the mucosa be injured. It has been shown in a number of experiments that cholecystitis is produced by direct extension from a previously inflamed liver. The richest supply of lymphatics is found immediately beneath the serosa. Cholecystitis secondary to hepatitis should be located at the periphery of the gall bladder. Most cases of gall-bladder infection show the pathologic condition at this site. The author also believes that this explains the frequency of vomiting in the early cases. This lymphatic connection also explains the association of cholecystitis with duodenal ulcer and appendicitis. However, he admits that there may be a few cases originating in the mucosa or due to contact infection. Kodama, of his laboratory, has shown that when the lymphatics of the gall bladder are injected with trypan blue, the colored solution appears in the first portion of the duodenum. If the lymphatics of the first portion of the duodenum are injected, the dve enters the gall bladder. If the lymphatics of the second or third portion are injected, the solution enters the mesenteric glands. He calls attention to these findings as having a bearing on the relationship of duodenal ulcer and cholecystitis.

Diagnosis.—In the majority of instances the clinical signs and symptoms are expressions of late effects of the disease. Therefore, other diagnostic means must be sought. This investigation has taken great strides since the advent of cholecystography, which is really a means of studying the function of the gall bladder rather than an indication of the exact pathologic lesion present. The author uses the intravenous method almost exclusively as he does not believe that the oral method is equally reliable.

Reactions have been few. In 150 cases, two have shown alarming symptoms, 65 per cent have experienced transient flushing, headache, dizziness, or vomiting. There is no danger of thrombophlebitis if the vein is washed out. Cholecystography is more accurate than inspection and palpation at operation.

Physiological considerations.—The question has been raised whether or not the bile flows out at the cystic duct. Use of the dye has demonstrated that the former is the procedure. By various experiments it has been shown, too, that it is unnecessary to assign much importance to the sphincter of Oddi; that the angle at which the common duct and pancreatic duct enter the duodenum and the muscular action of the latter explain the process of emptying of the duct. Also, the gall bladder itself empties by elasticity as a rubber bag would, and Graham and his co-workers have actually replaced a gall bladder in a dog by a rubber bag and by means of cholecystography have found it to act identically as the living gall bladder, with the exception of absorption of water and concentration of the dve.

ROBERT A. ARENS, M.D.

New Developments in Our Knowledge of the Gall Bladder. E. A. Graham. Am. Jour. Med. Sci., November, 1926, p. 625.

Routine roentgenologic gastro-intestinal examination.—This contribution has for its purpose a concise statement, to the general practitioner, of what he may expect from a routine gastro-intestinal X-ray examination. In relative frequency of occurrence the following conditions are commonly demonstrated: duodenal ulcer, appendicitis, adhesions, gastric carcinoma, gall-bladder disease.

In duodenal ulcer the X-ray is correct in 97 per cent of cases. The important findings are niche, spasm with deformity of the duodenum, hyperperistalsis, and spastic colon. Pyloric ulcer in the early stages gives rise to similar findings, but later there are added pyloric obstruction and gastric retention.

The lurking, backsliding, undetermined appendix gives rise to various findings, the chief of which are tenderness on palpation (with fixation or kinking), changes in shape or position, or beading (with delay in emptying).

Adhesions manifest themselves by the appearance of "hammocking," coils of bowel suspended from their extremities. In the pelvis the bowel may be bound into a glutinous mass, immovable by palpation under the fluoroscope. Then, again, a distended bowel may be seen suspended from bands, or bound down by adhesions.

Gastric carcinoma, in the well-advanced case, will show the well-marked filling defect. This finding is too late for treatment. Early findings should be emphasized. A stomach that presents a patent pylorus, with rapid emptying time, most likely harbors an early cancer and should be sent to the surgeon for exploration.

Gall-bladder diagnosis has been made more exact by the new method of Graham. Much importance should be attached to the indirect signs of gall-bladder disease, as shown by the X-ray. Their demonstration should always call for a careful examination by the Graham method. As our gall-bladder technic is thus perfected, more and earlier diseased gall bladders are being recognized and removed with increasing success.

Less frequent lesions are carcinoma of the large bowel, diverticulitis, tuberculous enterocolitis.

L. J. CARTER, M.D.

Expectations and Realizations from Routine Roentgenological Gastro-intestinal Examination. A. Stanley Kirkland. Can. Med. Assn. Jour., September, 1926, p. 1093.

Opaque material injected into sacral canal.

—In order to determine the levels reached by various caudal injections the author has injected an opaque substance into the sacral canal and immediately afterwards has obtained a photographic record of the fluid level by means of a roentgenogram.

When the opaque material was injected into the sacral canal of bodies within six hours after death, as for caudal anesthesia, it was found that 30 c.c. filled the canal to the fifth lumbar vertebra; 45 c.c. shows the fluid level at the upper border of the fourth lumbar vertebra; 60 c.c. at the seventh thoracic; 90 c.c. to the lower border of the fourth thoracic, and 120 c.c. to the third thoracic vertebra. In one case, when 120 c.c. had been injected, the roentgenogram showed that an escape of fluid had taken place into the external iliac vein and inferior vena cava. This would appear to indicate that absorption into the systemic venous system may occur from sacral canal injections under certain conditions. This fact has also been reported by Thompson.

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HOWARD P. DOUB, M.D.

X-ray Studies of Caudal Anesthesia and the Intravenous Absorption of Substances Injected into the Sacral Canal. David C. Elliott. Am. Jour. Surg., June, 1926, p. 139.

Acute abdominal conditions. - Hemorrhage, perforation, and stenosis are the most serious complications. Stenosis is slow in development, giving ample time for diagnosis, while hemorrhage and perforation are to be classed as surgical emergencies. The acute type of perforation demands urgent attention. The chronic type usually follows penetrating ulcers and the inflammation remains localized due to adhesions. Diagnosis may be made by X-ray examination or exploratory operation. Acute perforation is essentially a condition of the young adult, and mostly found in men. The diagnostic features are sudden, severe epigastric pain, board-like abdominal rigidity, and shock. Perforation may be preceded by a period of gastric disturbance or may occur without premonitory symptoms. With the development of peritonitis the original picture changes. Pain becomes generalized over abdomen instead of epigastric, and more acute when the patient is lying flat.

Vaughn has demonstrated that X-ray examination will show pneumoperitoneum within two hours in many cases, and X-ray study should be made if possible. X-ray examination will aid in ruling out one possible source of diagnostic error,—pneumonia. Other conditions which may require differential diagnosis are appendicitis, pancreatitis, cholecystitis, tabes, and mesenteric thrombosis.

Since acute appendicitis is the most com-

mon, it is well to remember that in upper tract perforations the outstanding symptoms are those due to peritoneal irritation and are sharply defined from the start, while in perforations of the lower tract the early symptoms are those of progressive sepsis.

Treatment is strictly surgical, and expectant treatment has no place in cases seen within the first twenty-four hours.

Summary.—(1) Perforations occur chiefly in young men with or without history of previous gastric disturbance.

- (2) Diagnosis is made by presence of severe epigastric pain, abdominal rigidity, and collapse.
- (3) Treatment is surgical and early operation is imperative.
- (4) The type of surgical procedure depends upon patient's condition, the type and location of the lesion and time that has elapsed.
- (5) The addition of posterior gastro-enterostomy lessens the likelihood of secondary operation.

C. H. DEWITT, M.D.

Acute Perforations of the Stomach and Duodenum. Franklin B. McCarty. Ill. Med. Jour., March, 1927, p. 224.

Short ultra-violet rays.—It is suggested to give the ultra-violet rays from 3,200 to 2,900 Ångströms the name "Dorno Rays," in honor of Professor K. Dorno, one of the outstanding investigators in this field.

E. A. Pohle, M.D.

The Short Ultra-violet Rays in the Sun Spectra. W. Hausmann. Strahlentherapie, 1926, XXIV, 192.

Hair ball.—The authors report a case of a man 35 years of age who had complained of distressing gastric symptoms for thirteen months. These symptoms were first noticed a few hours after eating persimmons, and consisted of severe epigastric pain, nausea, and vomiting, and later a boring and burning pain in the stomach, relieved by soda bicarbonate and food. Physical examination was negative except for a palpable mass in the epigastrium about the size of a lemon. Fluoroscopy showed a large defect in the stomach which had the appearance of a gas bubble and which changed its position on manipulation. On operation, a large hair ball made up of persimmon fibers was found. The authors then go into the differential diagnosis of this condition.

ROBERT A. ARENS, M.D.

Phytobezoar Diospyri Virginianæ: With Report of Case. William B. Porter and J. T. McKinney. Am. Jour. Med. Sci., November, 1926, p. 703.

Irradiation of the ovaries and its effect on the offspring.—During the last meeting of German Scientists and Physicians two reports were given regarding the possible injury to the future offspring by irradiation of the female generative organs. The reader is referred also to this Journal, 1926, VII, pp. 80, 81, where a series of articles on the same subject will be found.

Martius gives a very good review of the whole subject and concludes that no general rule can be established at present. The irradiation of the ovaries (temporary sterilization, fibroids during the child-bearing period, ovarian dysfunction, pelvic inflammatory diseases) must be done with great caution. It really comes to this: in each individual case, the physician has to balance the two possibilities, to help or to do harm; the decision as to whether therapy is indicated or not will, therefore, also rest with the individual gynecologist and radiologist.

Nuernberger's paper is recommended for study in the original. He states that, so far, nearly two hundred cases are known in which normal children have been born to previously irradiated women. He is convinced, however, that one has to differentiate in this problem between, first, ova fertilized between treatments and beginning of the roentgen amenorrhea, and second, those impregnated after the reappearance of the menstruation. It is pos-

sible that in the first group, damage may be done to the offspring, although positive cases have not been observed in man or animals. Normal offspring has been seen, however, in this group, in man as well as in animals. The injury to the offspring in cases of the second group has not been demonstrated so far. That, outside of this injurious effect on the first generation, one may expect injury to the following generation is highly improbable. It could, in any event, be only a recessive factor of inheritance which would make its appearance rather rarely, if practically possible at all. A good international bibliography supplements the article.

E. A. Pohle, M.D.

Irradiation of the Ovaries and Offspring. H. Martius. Strahlentherapie, 1926, XXIV, 101.

Irradiation of the Ovaries and Offspring. L. Nuernberger. Strahlentherapie, 1926, XXIV, 125.

Leukemia and infectious mononucleosis. Confusion exists in the diagnosis of several conditions associated with abnormalities of the white blood cells, chiefly because of the lack of uniformity in the choice of terms. Four cell types are concerned in these conditions:

1. The myeloblast is the only cell to which the term "mononuclear" should be applied; it is the most immature member of the series and occurs in the peripheral blood in leukemia.

2. The lymphoblast closely resembles the myeloblast, and requires special methods to distinguish it. It is the most immature form of the lymphatic series to enter the circulation. All gradations between this and the mature lymphocyte may be seen.

Lymphocyte refers to the mature deeply staining lymphocyte of normal blood; its younger forms are larger and with relatively more cytoplasm.

4. Monocytes are also called "endothelial leukocytes," "large mononuclears," and "transitionals." These terms should be dropped.

In acute leukemia, with large immature lymphocytes and lymphoblasts and a total count rising well above 50,000, there should not be confusion.

In infectious mononucleosis, which may be identical with what was formerly called "glandular fever" and is usually associated with Vincent's angina, there are marked blood changes. There is usually leukocytosis, which may be above 20,000, and is due to increase of the cells of the lymphocyte group, often 70 or 80 per cent being mature lymphocytes; however, sometimes there are a greater number of immature lymphocytes or even lymphoblasts, which lead to a suspicion of acute leukemia.

"Agranulocytic angina" is a recently coined term used to designate a condition of angina with leukopenia; this leukopenia affects the neutrophiles, leading to a relative lymphocytosis, which is sometimes incorrectly called "mononucleosis." Most of the cases have low total counts, but a few cases have been reported with normal or high counts for a part of the illness. This still further confuses the diagnosis.

W. W. WATKINS, M.D.

Concerning the Confusion between Acute Leukemia and Infectious Mononucleosis, with Report of a Case of Acute Lymphoblastic Leukemia, with Remission. H. P. Schenck and O. H. Perry Pepper. Am. Jour. Med. Sci., March, 1926, p. 320.

Cholecystography.—This paper was read before a group of general medical practitioners, and is a presentation of the status of the Graham-Cole method in the present-day diagnosis of gall-bladder conditions.

The writer's experience has been with the oral method only, which he has found simple and satisfactory. The dye, which is prepared according to the method described by the author in the August, 1926, number of Radiology, is placed in capsules immediately before it is given to the patient.

The ability to interpret correctly the findings shown by this method is dependent upon a thorough understanding of the normal functions of the gall bladder. This organ is not simply a reservoir to hold in reserve excess bile, since the amount of bile secreted by the liver in twenty-four hours is greatly in excess of the capacity of the gall bladder. The gall bladder, by means of its specialized mucous membrane lining, has the power of concentrating the bile to about one-tenth of its original volume. The gall bladder also acts as a regulator of the pressure within the ducts. It has in addition the power of muscular contraction by means of which it empties itself in response to the ingestion of a fatty meal.

In order that the gall-bladder functional dve test shall be possible, the liver secreting power must be intact, and the cystic and hepatic ducts must be patent. Any impairment of liver function or any narrowing or partial obstruction of the hepatic or cystic ducts will result in an absent or faint shadow. Failure of the concentrating power of the gall bladder would result in a faint shadow and would indicate a cholecystitis. Failure of the gall bladder to empty after a meal rich in fats would indicate loss of contractility and so point to cholecystitis, or would indicate obstruction of the common duct. Deformity of the gall-bladder shadow would indicate gallbladder disease. Mottling of the shadow would be evidence of gallstone complication.

L. J. CARTER, M.D.

The Present Status of Cholecystography. B. R. Mooney. Can. Med. Assn. Jour., December, 1926, p. 1461.

Pulmonary cancer.—The author gives an excellent summary of the subject, reporting four cases, only one of which had been autopsied. He notes the marked increase in the number of cases during the years of 1920 to 1922, inclusive, and suggests that this may be due to the late sequelæ of the influenza epidemic of 1918 and 1919. He mentions that the three accepted forms of treatment are surgery, radium, and high voltage X-ray, but that these have been without success except in a very few instances. The only possible chance of a cure lies in early diagnosis and lobectomy.

HOWARD P. DOUB, M.D.

Primary Carcinoma of the Lung. Henry W. Cave. Am. Jour. Surg., June, 1926, p. 141. A new roentgen therapy department.— Description of the new deep therapy department of the Medical Clinic at the University of Muenster. Protection of patients and personnel and dose measurements in accordance with the modern standards are discussed in detail.

E. A. Pohle, M.D.

The Roentgen Therapy Department of the Medical Clinic of the University of Muenster. P. Krause and C. Kruchen. Strahlentherapie, 1927, XXIV, 474.

Ureteral variations.—A girl, aged twelve, entered the hospital complaining of incontinence since birth. The physical examination was negative except for irritation of the external genitalia and upper inner aspect of the thighs. On cystoscopic examination nothing abnormal was seen except that the left ureter was inserted at a higher level. When indigo carmine was given intravenously, colored urine was seen to dribble from a small pinhead-size opening on the anterior vaginal wall about 1.5 cm. from the cervix. The opening was stretched and a small shadowgraph catheter was inserted. Pvelo-ureterograms were made of both kidneys and ureters and of the ectopic ureter. Left pyelogram was normal. The right kidney pelvis was rather small and the superior calyx broad. The catheter inserted into the ectopic ureter passed up a short distance then coiled up in a cystic dilatation. The ureter above this dilatation was tortuous and dilated and ended in a rudimentary pelvis.

On operation the kidney was found to be unusually long. A shallow sulcus was located on the anterior surface. The upper segment was drained by a large pelvis and a dilated ureter and had a separate blood supply. A heminephrectomy was done.

Examination of the literature showed 100 cases, divided as follows:

- Single ureter with ectopic opening, 24 cases.
 - 2. Complete unilateral duplication of pelvis

and ureter, with ectopic opening of supernumerary ureter, 55 cases.

- 3. Complete unilateral duplication of pelvis and ureter, with ectopic opening of both ureters, 2 cases.
- 4. Supernumerary kidney pelvis and ureter, with an ectopic opening, 2 cases.
- 5. Bilateral duplication of pelves and ureters, with one ectopic opening only, 14 cases,
- 6. Bilateral duplication of pelves and ureters, with bilateral ectopic openings, 2 cases.
- 7. Both single ureters having ectopic opening, 1 case.

ROBERT A. ARENS, M.D.

Ectopic Ureteral Openings: Report of Case. Robert H. Herbst and Hugh J. Polkey. Jour. Urol., January, 1927, p. 61.

American and German roentgen units.— The authors compared six ionization instruments calibrated in German roentgen units with their own and those of other American investigators. They found that the German unit is approximately 50 per cent higher than the average American unit. Multiplying an erythema dose by 0.57 or 0.66 will lead to the respective dose in German units. For deep therapy, for instance, 900 R (in air) American units are equal to 600 R German units.

E. A. Pohle, M.D.

Erythema Doses in Roentgen Units. Otto Glasser and William H. Meyer. Strahlentherapie, 1927, XXIV, 710.

Sensitization to secondary roentgen rays.

—The attempt has often been made to increase the effect of radiation by introducing elements of high atomic number in order to create a sensitization towards secondary radiation. Well known are the experiments of Ghilarducci, Halberstaedter and Meyer, Liechti and Friedrich. It is possible, for instance, to multiply the effect of rays on a culture of bacteria by exposing it to the secondary radiation of lead. The authors present in this paper an amount of valuable material,

based upon their own investigations dealing with the action of secondary radiation (secondary electrons and true radiation) on photographic films and cultures of Bacillus prodigiosus. The study of the relation between the wave length of primary rays and atomic number of the element emitting secondary radiation (true radiation, photo and recoil electrons) gave different results when using the ionization, photographic, and biological method of investigation. In either case there is a combined effect of all three types of secondary radiation in evidence. It is impossible in an abstract to do justice to this important work: the reader is referred to the original for details. One practical conclusion should be mentioned: there is no chance at present of increasing the effect of radiation in the human body by introducing elements of high atomic number into the tissue.

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E. A. Pohle, M.D.

Sensitization to Secondary Rays from Metal Surfaces; Experiments with Photographic Emulsion and with Superficial Cultures of Bacteria. H. Holthusen, A. Schuback, and H. Sielman. Strahlentherapie, 1927, XXIV, 577.

Cancer of the tongue.-The author considers that a primary cancerous lesion confined to the tongue may be satisfactorily treated by deep radium therapy. If, however, the lesion is quite small and at the tip of the tongue, it is better, both for diagnostic and therapeutic reasons, to excise freely. Where necrosis has followed unsuitable radium treatment it is useless to continue it, and it is better to proceed surgically. Penetrating radiotherapy, either alone or associated with radium puncture, is said to be unable to cure cancer of the tongue, and still less the glandular metastasis; in advanced cancer, with palliative irradiation, it is useful. For enlarged and definitely cancerous glands external and

deeply penetrating radium therapy is more effective than surgery. Zanotti adds that it should be remembered that a large percentage of the glands removed (40 per cent, according to Poirier) are not cancerous. Where the glands are bulky it is advisable to excise as much as possible as a preliminary to the radium treatment, but if the glandular enlargement is not marked radium therapy alone will suffice. Treatment by local radium puncture. with external application, should be simultaneous and continuous, using screened tubes of 2 mm. and 1 mm. platinum, respectively. The dose should be weak, but capable of destroying cells in mitosis. If less screened tubes are used, it is better to divide the treatment into two stages, so as to avoid the risk of necrosis. Sterilization of the tumor by long-continued treatment according to the method of De Nabias is generally preferable. Since the radium treatment of lingual cancer is so full of technical difficulty it should be given in a properly equipped hospital.

Radiotherapy for Cancer of the Tongue. G. Zanotti. Il Policlinico, Sez. Chir., January 15, 1927, p. 34. (Reprinted by permission from Brit. Med. Jour., March 19, 1927, p. 55 of Epitome of Current Medical Literature.)

Roentgen therapy of gastric ulcer.—The authors have treated twelve cases of gastric ulcer with roentgen rays (160 K.V., 1.0 Cu., 50 cm. F.S.D., 10×10 cm. anterior field, 4 H per field). Only six cases were under observation more than one year. The treatment of all acute ulcers and those chronic cases without obstruction is recommended; hemorrhage does not contra-indicate irradiation.

E. A. Pohle, M.D.

X-ray Therapy of Gastric Ulcer. V. Schiller and W. Altschul. Strahlentherapie, 1927, XXIV, 736.

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